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The January Number of the *Medical Clinics of North America* comes from Chicago.—It includes a 9-Clinic *Symposium on Pneumonia*—a wealth of clinical help which the Family Physician will find useful in his everyday practice. There are clinics on Pathogenesis of Pneumonia, Early Diagnosis and Specific Treatment of Lobar Pneumonia, Pulmonary Disease Secondary to Amebiasis, Diagnosis and Differential Diagnosis of Pneumonia, Differential Diagnosis of Pneumonia in Childhood, Medical Diathermy in Pneumonia, Treatment of Empyema, Use of Oxygen in Pneumonia, and the Bronchoscopic Aspects of "Unresolved Pneumonia".

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THE USE AND INTERPRETATION OF TESTS FOR LIVER FUNCTION

A CLINICAL REVIEW

ALBERT M. SNELL, M.D.
AND
THOMAS B. MAGATH, M.D.
ROCHESTER, MINN.

For twenty years or more clinicians, physiologists and clinical pathologists have attempted to devise procedures or tests that would indicate the functional capacity of the liver, in order to determine the presence and degree of disease of the liver and to obtain information with regard to prognosis. The careful physiologic studies that have been made following total and partial hepatectomy have served as a guide to the solution of this problem and have stimulated interest in it. Meanwhile, physiologists repeatedly have warned that no one function could be depended on to indicate the general status of the whole organ and that the reserve function of the liver was so great that functional abnormalities could be expected to appear only when most of it had been destroyed. In presenting the following report, it is our intention to consider the utility and general significance of the tests in common use and to place a minimum of emphasis on the theoretical and other phases of the problem. Only the clinical aspects of the subject and reliability of the tests from the standpoint of observed pathologic changes will be considered. The material comprises several thousands of the various tests performed within a period of about five years on the medical and surgical patients of the Mayo Clinic and its allied hospitals. References to the voluminous literature on the subject have been largely omitted and those interested in the physiologic aspects of the various procedures are referred to the excellent reviews by Soffer [1] and by Rich.[2]

SERUM BILIRUBIN

Just as determinations of values for the blood urea or nonprotein nitrogen are the most useful and reliable methods of determining the functional efficiency of the kidney, so does the determination of the value for the serum bilirubin provide useful information with regard to the functional status of the liver. The earlier work of Mann, Bollman and Magath [3] on hepatectomized animals indicated that the liver acts as an excretory organ with respect to bilirubin just as the kidney does for urea. On this basis it is possible to attribute increases of serum bilirubin to three general types of disturbances which act singly or in combination: (1) those in which bilirubin is produced in excess of the capacity of the liver to excrete it (hemolytic jaundice); (2) those in which the rate of production is not increased but because of toxic or infectious injury to the liver cells and finer bile passages bilirubin accumulates in the blood stream (hepatogenous jaundice); (3) those in which obstruction to the larger bile passages causes a reflux of bilirubin into the blood (obstructive jaundice). As Rich [2] has argued, the presence of increased amount of bilirubin in the blood because of excess production of bilirubin does not depend on this fact alone but depends in part on an associated disturbance in the excretory function of the liver cells. Actually, the argument can be carried further and extended to prove that pure forms of one or the other types of jaundice are probably rare. There is never gross obstruction to the extrahepatic bile passages without injury to the hepatic parenchyma; conversely, there is never a pure hepatic form of jaundice without injury or obstruction to the finer bile passages. One may however say that jaundice is preponderantly hemolytic, hepatogenous or obstructive, depending on whether one is dealing with a blood dyscrasia, a lesion of the hepatic parenchyma or a lesion which obstructs the flow of bile in the extrahepatic duct system; this conception of the three distinct varieties of jaundice, while technically objectionable, is of too great clinical usefulness to be discarded.

The Thannhauser-Andersen [4] modification of van den Bergh's original method has been used in our determinations; the report gives the total bilirubin present and its reaction (direct or indirect). For practical purposes it may be considered that the bilirubin ordinarily present in the serum gives the "indirect" reaction and may exist in amounts varying from 0.1 to 2.0 mg. per hundred cubic centimeters, according to the method of determination. In hemolytic icterus and in the hemolytic anemias, the excess of bilirubin is apparently "bound" in the blood stream and is not eliminated by the kidney. It gives an indirect reaction and the total quantity rarely exceeds from 6 to 7 mg. per hundred cubic centimeters of serum. Whether this indicates an impairment in liver function is not entirely clear, although associated visible hepatic injury of significant degree is rarely demonstrated. However, if the value for the indirect-reacting bilirubin reaches a level of more than 4 mg. per hundred cubic centimeters of serum it may be safely assumed that the function of the cells of the liver has been at least functionally impaired.

From the Division of Medicine (Dr. Snell) and the Division of Clinical Pathology, Section on Parasitology (Dr. Magath), the Mayo Clinic.

1. Soffer, L. F.: Present Day Status of Liver Function Tests, Medicine **14**: 185-254 (May) 1935.
2. Rich, A. R.: The Pathogenesis of the Forms of Jaundice, Bull. Johns Hopkins Hosp. **47**: 338-377, 1930.
3. Mann, F. C.; Bollman, J. L., and Magath, T. B.: Studies on the Physiology of the Liver: IX. The Formation of Bile Pigment After Total Removal of the Liver, Am. J. Physiol. **69**: 393-409 (July) 1924.
4. Thannhauser, J. S., and Andersen, E.: Methodik der quantitativen Bilirubinbestimmung im menschlichen Serum, Deutsches Arch. f. klin. Med. **137**: 179-186, 1921.

If the serum shows the presence of a direct-reacting bilirubin it is practically conclusive proof of injury of the liver and rupture of bile capillaries. In other words, the bilirubin which is taken out of the blood serum as a result of physiologic or mechanical obstruction is being reabsorbed through lymphatic channels while a part at least may pass back into the circulation through the polygonal cells of the liver.

If the van den Bergh test is carefully performed as a ring test instead of a "mixture" test, one may often detect a direct reaction even though there is only the slightest increase in the total amount of bilirubin in the serum. This is an important point which has not been generally recognized. There is no doubt that the presence of direct-reacting bilirubin has some quantitative relation to the function of the liver, that at a certain point the functional or pathologic changes become so great that the cells of the liver are forced to return some of the pigment; in this way high values for indirect-reacting bilirubin tend to give way to the presence of a direct-reacting bilirubin. This is typically seen in jaundice due to arsphenamine, in which the van den Bergh reaction is indirect at first but later is direct.

As a practical matter, one may expect direct van den Bergh reactions in about 80 per cent or more of cases in which there is even a moderate degree of hepatic injury, while one may expect a direct reaction in only about 1 per cent of all cases in which there is an absence of clinical evidence of injury of the liver. A point which has been overlooked is the fact that in serums which give a direct reaction there is also a varying amount of indirect-reacting bilirubin and hence in studying jaundiced patients better correlations might be had if one could determine the amount of both types of bilirubin present, rather than considering that all bilirubin was of the "direct" type. Numerous investigators, for example Heilmeyer and Krebs [5] and Bengolea, Velasco Suárez and Raices,[6] have indicated that this separation can be made and that the direct-reacting fraction is smaller than one might anticipate. Biphasic reactions therefore probably represent conditions in which there is little direct-reacting bilirubin as compared with the amount of the indirect-reacting pigment.

In clinical practice, one encounters indirect reactions in the following conditions: pernicious anemia, familial hemolytic jaundice, acute hemolytic anemia, sickle-cell anemia, paroxysmal hemoglobinemia, transfusion of the wrong type of blood, phenylhydrazine poisoning, cardiac decompensation (especially in the presence of gross pulmonary infarction), hemolytic septicemia, malaria, blackwater fever, lobar pneumonia and icterus neonatorum. It is important to recall that these conditions as a rule are associated with a typical acholuric jaundice and that deep jaundice and high values for bilirubin are rarities unless the liver also is injured.

Direct-reacting bilirubin is present in the serum under the following conditions: various types of toxic or infectious jaundice; chronic parenchymatous disease of the liver; mechanical obstruction to bile ducts by tumor, stone, cicatrix, infectious lesions or extrinsic pressure, or tumors, granulomas, cysts and other lesions involving the liver substance. The relative depth of jaundice in these various types of cases may be noted here. The highest values for serum bilirubin (from 30 to 50 mg. per hundred cubic centimeters) are found in acute severe hepatogenous forms of jaundice and in neoplastic biliary obstruction; intermediate values (from 10 to 30 mg. per hundred cubic centimeters) are found in the milder degrees of hepatic parenchymal lesions and in conditions in which intermittent or partial biliary obstruction exists; the lower grades of bilirubinemia (from 2 to 10 mg. per hundred cubic centimeters in the presence of a direct van den Bergh reaction) are found in subsiding acute "intrahepatic" jaundice, in very chronic forms of hepatitis such as those which sometimes follow biliary obstruction or prolonged intrabiliary infection, and in the various forms of portal cirrhosis and syphilitic hepatitis, in the presence of a stone in the common bile duct, and in infectious forms of cholecystitis without gross biliary obstruction.

Having determined the reaction of the patient's serum to the van den Bergh test and the degree of bilirubinemia, one has still to consider the practical problem of the daily variations of jaundice, since the condition is rarely static. This may be done by the continued use of the tests which have been mentioned or by the comparison of the color of the serum with that of a standard solution of potassium dichromate, in order to determine the so-called icterus index. The results of the last method, while not strictly comparable to the results of chemical determination of bilirubin, may be clinically useful. Plotted as a curve [7] such determinations may be of some diagnostic and prognostic value. In complete biliary obstruction due to neoplasm, a rapidly rising curve is the rule, especially if the gallbladder has been previously removed or has been rendered nonfunctioning by local disease. If the organ is intact, the abrupt rise is converted into a slow and gradual one. If obstructive biliary cirrhosis supervenes, as is so frequently the case in the presence of stricture or stone in the common bile duct, a low plateau curve is the rule; if the liver is not extensively affected, as is the rule in recent neoplastic obstruction, a high plateau curve results; later, a gradual fall in the value for the bilirubin may occur. Studies on dogs which had been subjected to experimental ligation and section of the common bile duct demonstrated an interesting parallelism to these observations. In any large group of cases of jaundice one recognizes certain other types of curves which are clinically significant. Acute "intrahepatic" forms of jaundice produce a rapid rise and an equally rapid fall in the values for the bilirubin; the longer the peak values are maintained, the slower is the decline. In chronic parenchymatous disease of the liver low irregular curves are the rule, exactly as they are in cases of long-standing biliary obstruction; in either instance, episodes of rapid degeneration of liver tissue may be marked by sustained rises in the values for the bilirubin. In general, falling curves for the values for bilirubin signify restored patency of the bile passages or a liver that is undergoing repair; the one exception is the very chronic type of biliary obstruction. High or rising values, as a rule, signify complete obstruction, a rapidly degenerating hepatic parenchyma or a combination of the two.

DETERMINATIONS OF UROBILIN AND UROBILINOGEN

The bilirubin which enters the intestinal tract is acted on by bacteria to form urobilinogen; this is ordinarily returned to the liver and utilized in the formation of

5. Heilmeyer, Ludwig, and Krebs, Willy: Spektrophotometrische Untersuchungen des Ehrlich-Pröscherschen Bilirubin-Azofarbstoffes und ihre praktische Anwendung, besonders zur quantitativen Bestimmung des Bilirubins im Blutserum, Biochem. Ztschr. **223**: 352-364, 1930.

6. Bengolea, A. J.; Velasco Suárez, C., and Raices, A. E.: El dosaje de la bilirrubina directa e indirecta en el suero sanguíneo: Su importancia en cirugía hepato-biliar, Prenza méd. Argentina. **23**: 85-102 (Jan. 8) 1936.

7. Snell, A. M.: Hepatic Parenchymal Lesions and Hepatic Function of Patients with Obstructive Jaundice, Tr. Am. Gastro-Enterol. A., 1932, pp. 196-223.

normal body pigments. In the presence of hepatic injury this resynthesis may be halted and urobilinogen therefore may be excreted in the urine. If the bile passages are completely obstructed, no bilirubin reaches the bowel and consequently no urobilinogen can be formed. Because of the difficulty of making quantitative determination of urobilin and urobilinogen in urine and feces, the use of this knowledge as a test for hepatic function has not enjoyed widespread use. A limited amount of information, however, can be gained by single qualitative or crude quantitative tests for the presence of these substances in the urine. Urobilin is not excreted as such in the urine but may be demonstrated by exposing the urine to sunlight, either direct or diffuse, when any urobilinogen will be converted to urobilin. Indeed, if the presence of urobilinogen is to be detected by ordinary means the urine must be very fresh. Therefore it is best to convert all the urobilinogen into urobilin and determine the latter quantitatively. In neoplastic obstruction to the bile passages there is usually an absence of urobilinogen in the urine, but bilirubin is present; while, in hepatogenous jaundice, urobilinogen and bilirubin are both present. In hemolytic icterus, even though the urine contains no bile pigment, urobilinogen is present. During the course of epidemic or catarrhal jaundice an interesting phenomenon is observed: only at the beginning and at the end of the disease is urobilinogen found, probably because during the height of the course of the disease there is sufficient injury to interrupt the continuity of the finer bile passages.

In general, as Watson [8] has shown, much more conclusive information with regard to urobilin and urobilinogen metabolism can be obtained by quantitative studies of the fecal and urinary excretion of these substances during definite test periods; such studies, while hardly applicable for general use, show that the amounts of bilirubin entering the intestine and therefore the quantity of urobilinogen formed from day to day vary considerably and thus render single examinations of the urine of doubtful diagnostic significance.

There is one interesting recent development with regard to a product of hemoglobin destruction which is affected by disease of the liver. It has been shown that some forms of coproporphyrin are excreted by the kidney in excess when the liver is injured; the same substance may accumulate in the liver during periods of biliary obstruction and may be excreted in the bile as obstruction is relieved. Further investigations along this line may result in additional methods of studying hepatic function with respect to porphyrin metabolism.

TESTS DEPENDING ON THE GENERAL PROPERTIES OF THE LIVER WITH RESPECT TO INTERMEDIARY METABOLISM

Protein Metabolism.—The effect of total hepatectomy on the metabolism of certain protein derivatives is of theoretical interest, as Bollman, Mann and Magath [9] have shown. The removal of the liver is followed by a rapid fall in the concentration of the urea in the blood, urine and tissues, which indicates that the formation of urea has ceased. Amino nitrogen accumulates at the same time, but the increase is masked because of the absorption of these substances by muscular tissues. In the dog there is a rise in the uric acid content of the tissues and body fluids, and the tolerance to injected uric acid is reduced. A partial hepatectomy, or Eck fistula, does not produce changes of the same degree and therefore one would hardly expect that significant alterations could be noted in the ordinary case of disease of the liver. In animals which have been subjected to experimental ligation of the common bile duct, in occasional cases of obstructive jaundice or, more commonly, in cases of acute yellow atrophy, there may be a fall in the concentration of blood urea and nonprotein nitrogen; but any other defects in protein metabolism are difficult to demonstrate. Earlier studies of nitrogen partition in the urine revealed some minor changes in intermediate protein metabolism in cases of liver disease; in one case studied at the Mayo Clinic there was evidence of decrease in the formation of urea and increase in amino acid nitrogen content of both blood and urine. These values returned to normal as the patient improved but were of insufficient magnitude to be of much clinical importance.

So far as tests of liver function calculated to test the protein metabolism are concerned, little has been done which is clinically significant. One test which has been advocated consists of the administration of 50 Gm. of gelatin and the subsequent quantitative examination of the urine for amino acids. In normal persons the excretion is prompt, and at least 200 mg. of amino acid is present in the first four hour period; in the presence of disease of the liver there is considerable delay in excretion and the amount of amino acid in the earlier specimens of urine is small. We have had no experience with this method of study and would not expect it to yield information of great practical value when performed on man.

There is one phase of protein metabolism which is not strictly related to the matter which has just been considered but which is of considerable importance from a clinical standpoint. We refer to the variations in the plasma proteins which have been recognized as dependent on injury to the hepatic parenchyma. While there is no direct proof that the liver is the sole site of their manufacture, experimental studies furnish some indirect evidence of their possible hepatic origin. Kerr, Hurwitz and Whipple [10] demonstrated that poisoning with phosphorus and carbon tetrachloride resulted in a moderate decrease in the value for the serum proteins and also that regeneration of serum protein, after plasmapheresis, occurred slowly in the presence of hepatic injury or of an Eck fistula. Recent work in Whipple's (Holman, Mahoney and Whipple [11]) laboratory indicated that there is a reserve of protein-building material in the organism, which is stored, at least in part, in the liver and which probably consists of at least 50 per cent of albumin or albumin-producing material. These investigators recently expressed the opinion that there probably is a dynamic equilibrium between tissue and plasma protein, and the material stored in the liver may figure in this equilibrium.

There is a long series of reports on the relation of hepatic disease to the value for the serum protein; the

8. Watson, C. J.: Studies of Urobilinogen: I. An Improved Method for the Quantitative Estimation of Urobilinogen in Urine and Feces, Am. J. Clin. Path. **6**: 458-475 (Sept.) 1936.

9. Bollman, J. L.; Mann, F. C., and Magath, T. B.: Studies on the Physiology of the Liver: VIII. Effect of Total Removal of the Liver on the Formation of Urea, Am. J. Physiol. **69**: 371-392 (July) 1924; Studies on the Physiology of the Liver: X. Uric Acid Following Total Removal of the Liver, Am. J. Physiol. **72**: 629-646 (May) 1925.

10. Kerr, W. J.; Hurwitz, S. H., and Whipple, G. H.: Regeneration of Blood Serum Protein: II. Influence of Diet upon Curve of Protein Regeneration Following Plasma Depletion, Am. J. Physiol. **47**: 370-378 (Dec. 1) 1918; Regeneration of Blood Serum Proteins: III. Liver Injury Alone: Liver Injury and Plasma Depletion: The Eck Fistula Combined with Plasma Depletion, ibid. **47**: 379-392 (Dec. 1) 1918.

11. Holman, R. L.; Mahoney, E. B., and Whipple, G. H.: Blood Plasma Protein Given by Vein Utilized in Body Metabolism: II. A Dynamic Equilibrium Between Plasma and Tissue Proteins, J. Exper. Med. **59**: 269-282 (March) 1934.

literature on the subject has been cited recently by Myers and Keefer.[12] It has been observed repeatedly that in advanced chronic hepatic lesions there is a moderate reduction in the value for the serum proteins; the diminution occurs chiefly in the albumin fraction and there is a reversal of the albumin-globulin ratio. In the presence of less advanced lesions, the amount of albumin may be only moderately reduced and the amount of globulin may be normal or increased. In any type of hepatic disease, however, the effects on the albumin-globulin ratio are somewhat the same. In some cases of advanced cirrhosis observed at the clinic the albumin-globulin ratios were as low as 0.3; in less serious types of cirrhosis the changes in the ratio are not marked or constant, and the variations noted tend to return to normal as improvement takes place. In all but a few of a fairly large series of cases of all types of hepatic disease, the albumin-globulin ratio has been disturbed considerably but there was not much reduction in the value for the total proteins. The rapidity with which changes in the amount of total protein and in the albumin-globulin ratio may take place is rather striking, and repeated determinations in the same case indicate that these changes may not be without some prognostic significance.

Peters and Eisenman[13] have properly raised the objection that such variations in serum proteins may be of nutritional origin and may not be attributable to failure of production of protein by the liver. However, the rapidity with which variations occur is not easily explained on a nutritional basis, and it also is known that in cases of hepatic disease feeding with protein has little effect on either the value for the serum protein or the albumin-globulin ratio. Similar observations have been made in cases of intermittent obstructive jaundice in which diets of known composition were used. Likewise, in cases of portal cirrhosis and ascites the amount of protein lost in ascitic or edema fluid does not seem to be important. In general, the clinical and experimental evidence related to decrease in the amount of serum proteins in cases of hepatic injury seems to indicate a failure of production of protein or protein-building substances on the part of the liver, and an altered equilibrium between circulating and stored protein.

The principal effects referable to the reduced albumin content of the blood serum of patients who have hepatic disease are obviously related to the production of ascites and edema. It is probable that ascites in hepatic disease does not depend necessarily on the value for the serum proteins alone but that such factors as portal venous stasis and chronic peritoneal irritation play an important part. The decrease in the amount of serum albumin is, however, a most important contributing factor, which may reduce the osmotic pressure enough to allow transudation under certain conditions (Snell and Maclay[14]).

Fat and Cholesterol Metabolism.—It has been known for many years that in the presence of parenchymatous disease of the liver, or even following acute toxemias and infections, the amount of fat in the individual hepatic cells is greatly increased and the glycogen content is diminished at the same time. This, of course, does not necessarily imply that the liver is directly concerned in the regulation of fat metabolism, although some indirect connection of this sort cannot be excluded. It is also known that in obstructive jaundice, when bile is completely excluded from the intestinal tract, fats are absorbed poorly. The hemokonia test of Brulé[15] was based on this observation and by the use of this test it is possible to demonstrate a failure of any increase in the microscopic particles of blood fat which normally appear after a mixed meal. Unfortunately, the test reveals little more than can be learned by examination of the stools and duodenal contents and hence is not clinically important.

A study of the cholesterol and cholesterol esters in the plasma in various types of disease of the liver has been carried out in various institutions for many years, and many men prominent in the field of medicine have contributed information bearing on this subject. In a recent article Epstein and Greenspan[16] summarized the entire matter very well and those interested are referred to this article for details. We have records of a rather large number of determinations of cholesterol and cholesterol esters in the plasma of patients who had various types of biliary obstruction and parenchymatous disease of the liver; the results in general confirm those which have been reported by these and other writers. In obstructive jaundice there is usually a sharp rise in the values for both the cholesterol and the cholesterol esters, which may be roughly parallel to the elevation of the value for the serum bilirubin. If biliary obstruction of long duration, cholangeitis or obstructive biliary cirrhosis complicates the picture, the value for the cholesterol in the plasma may be normal or decreased. In cases in which acute parenchymatous disease of the liver is associated with jaundice, the value for the cholesterol may be decreased or normal and that for the cholesterol esters may be diminished or these esters actually may be absent. It has been thought that the value for the cholesterol esters gives some idea of the severity of the injury to the liver and of the prognosis, but in our experience this has not been entirely substantiated. In the ordinary types of portal cirrhosis the value for the cholesterol usually is normal except when acute degeneration of the liver supervenes. As Epstein and Greenspan[16] have wisely remarked, in evaluating a single determination of the amount of cholesterol in the plasma it is important to consider the clinical sequence of events and to make allowances for the stage of the disease and for the possible existence of infectious or extrahepatic disease which might influence the results.

Carbohydrate Metabolism.—The most significant result of experimental hepatectomy perhaps is the decrease in the value for the blood sugar and the hypoglycemic reaction which continues because the normal store of glycogen in the liver is abolished. If the capacity of the liver to maintain the normal amount of blood sugar is one of the most important functions of this organ, it is perhaps to be expected that this function would be conserved to the very end in the presence of disease of the liver. This seems to be the case and for this reason functional tests of carbohydrate metabolism have been disappointing in practice. In advanced hepatic injury from whatever cause, hypoglycemia is

12. Myers, W. K., and Keefer, C. S.: Relation of Plasma Proteins to Ascites and Edema in Cirrhosis of the Liver, Arch. Int. Med. **55**: 349-359 (March) 1935.

13. Peters, J. P., and Eisenman, Anna J.: The Serum Proteins and Diseases Not Primarily Affecting the Cardiovascular System or Kidneys, Am. J. M. Sc. **186**: 808-833 (Dec.) 1933.

14. Snell, A. M., and Maclay, Elizabeth: The Effects of Chronic Disease of the Liver on the Composition and Physicochemical Properties of Blood: Changes in the Serum Proteins; Reduction in the Oxygen Saturation of the Arterial Blood, Ann. Int. Med. **9**: 690-711 (Dec.) 1935.

15. Brulé, Marcel: Recherches sur les ictères: les rétentions biliaires par insuffisance hépatique, ed. 3, Paris, Masson et Cie, 1922.

16. Epstein, E. Z., and Greenspan, E. B.: Clinical Significance of the Cholesterol Partition of the Blood Plasma in Hepatic and in Biliary Diseases, Arch. Int. Med. **58**: 860-890 (Nov.) 1936.

but rarely seen; a hypersensitiveness to insulin has been noted, and one sees an occasional hypoglycemic reaction in cases in which diabetes and hepatic disease are coexistent. Likewise, it has been noted that when obstructive jaundice or cirrhosis is associated with severe diabetes, the glycosuria becomes easier to control and the administration of insulin is no longer necessary; as the hepatic lesion improves, a return to the earlier status is to be expected. Insulin, water and standard doses of dextrose have been given simultaneously and the values for the blood sugar have been studied at intervals thereafter (Althausen and Mancke [17]); by this method it is sometimes possible to show variations in the values for the blood sugar which indicate a low glycogen reserve and which tentatively point to the presence of hepatic injury. Our experience with this test is limited, but in general we may say that it has not as yet been generally employed or accepted; the principal objections obviously are based on possible variations in the nutritional state of the patient to be tested, and these variations may influence the result.

Two other sugars, levulose and galactose, have been widely used in the study of hepatic function; their employment is based on the fact that the normal liver can utilize them for storage (as glycogen) without producing significant glycosuria or hyperglycemia. The levulose tolerance test, as advanced by MacLean and de Wesselow,[18] had its inception in Schirokauer's [19] observation that the value for the blood sugar of normal persons was virtually unaffected by the oral administration of levulose, whereas it was increased in the presence of hepatic disease. In performing this test we have administered a standard dose of 40 Gm. of levulose in 200 cc. of lemonade; the value for the blood sugar was determined one and two hours later; an increase of more than 30 mg. per hundred cubic centimeters in the value for the blood sugar is considered indicative of a positive test. Space prohibits a detailed consideration of the results. When the test was performed on experimental animals and all outside influences were excluded, the results were reasonably reliable; but when it was performed on patients, many difficulties and errors were encountered. A low initial value for the fasting blood sugar, mild diabetic tendencies, and chronic pancreatic disease all tend to vitiate the results. There is no doubt that rather consistent results may be obtained under ideal conditions, particularly if the value for levulose in the blood is determined; in general, however, the field of usefulness for this test is limited.

Galactose tolerance tests have had an even greater vogue in clinical medicine, especially in European clinics; the test is based on the observation that a normal person can assimilate a 40 Gm. oral dose of galactose without the loss of more than from 2.5 to 3 Gm. of sugar in the urine in the five hours immediately following the administration of the galactose. In the presence of hepatic injury, conversion of this sugar into glycogen fails sufficiently to allow for a degree of glycosuria above this arbitrary level. As advocated in Germany by Bauer [20] and in this country by Shay and Schloss,[21] the test has been used to distinguish intrahepatic jaundice from obstructive jaundice; a positive test is said to denote parenchymatous damage, a negative one supposedly indicates a substantially normal hepatic parenchyma. Actually, as Banks and his co-workers [22] showed, there are two serious stumbling blocks: the test is consistently negative in portal and biliary cirrhosis and is positive in from 25 to 40 per cent of cases in which obstructive jaundice has persisted for a sufficiently long time to injure the hepatic parenchyma. In rather acute conditions associated with jaundice, a positive test is a strong argument for a primarily hepatic lesion; this is especially true in cases in which injury of the liver is produced by cinchophen derivatives, but even in this group of cases the results occasionally are negative. In cases of chronic jaundice the results show a large margin of error and therefore we may say that the test is not an infallibly reliable guide in differentiating obstructive jaundice from "intrahepatic" jaundice. So far as we have been able to determine, the test has no value whatever in cases in which the patients are not visibly jaundiced.

TESTS OF EXCRETORY FUNCTION

Although a large number of dyes have been used to test the excretory function of the liver, only two, rose bengal and bromsulfalein, have come into common use.

The rose bengal test is done without reference to the weight or age of the patient or to the amount of dye administered (Stowe, Delprat and Weeks [23]). The standard is obtained from a sample of blood drawn two minutes after the dye is injected; a sample of blood drawn exactly eight minutes after injection is compared with the standard. Normally, 50 per cent or less of the injected dye (usually from 0.1 to 0.2 Gm.) should be present in the blood eight minutes after the injection has been made. Retention of more than that amount is considered an indication of hepatic damage. Since the dye has a photosensitizing effect, the specimens should be kept in the dark and the patient should be protected from direct sunlight for some hours after the use of the dye. Analysis of results by others show that the test gives results comparable to those obtained by the bromsulfalein test. Certain difficulties, such as the obtaining of a satisfactory standard, adequate mixing of the dye in the blood stream, and the rigid time requirements of the test, are self evident.

The bromsulfalein test, which perhaps is the most generally satisfactory test for hepatic function yet devised, is simple in the extreme. As first proposed, a dose of 2 mg. of the dye per kilogram of body weight was injected and specimens were obtained at five minutes, thirty minutes and one hour thereafter. O'Leary, Greene and Rowntree [24] first showed that the test could be improved by injection of 5 mg. of the dye per kilogram of body weight, and Magath [25] further simplified the test by taking a single specimen at the end of one hour. More than 10,000 tests have been performed at the clinic by this method. The amount of dye present

17. Althausen, T. L., and Mancke, R.: Kombinierte Leberfunktionsprüfung (Insulin-, Glykose- und Wasserbelastung), Arch. f. klin. Med. **170**: 294-301 (March 25) 1931.
18. MacLean, H., and de Wesselow, O. L. V.: The Estimation of Sugar Tolerance, Quart. J. Med. **14**: 103-119 (Jan.) 1921.
19. Schirokauer, Hans: Zur Funktionsprüfung der Leber: Die alimentäre Lävulose-Hyperglykämie, Ztschr. f. klin. Med. **78**: 462-475, 1913.
20. Bauer, Richard: Unsere Kenntnisse über Leberfunktion und ihre Verwertung für die Klinik, Wien. klin. Wchnschr. **45**: 1577-1581 (Dec. 23) 1932.
21. Shay, Harry, and Schloss, Eugene: Painless Jaundice: Its Differential Diagnosis by the Galactose Tolerance Test, J. A. M. A. **98**: 1433-1436 (April 23) 1932.
22. Banks, B. M.; Sprague, P. H., and Snell, A. M.: Clinical Evaluation of the Galactose Tolerance Test, J. A. M. A. **100**: 1987-1993 (June 24) 1933.
23. Stowe, W. P.; Delprat, G. D., and Weeks, Alanson: The Rose Bengal Test of Liver Function, Am. J. Clin. Path. **3**: 55-60 (Jan.) 1933.
24. O'Leary, P. A.; Greene, C. H., and Rowntree, L. G.: Diseases of the Liver: VIII. The Various Types of Syphilis of the Liver with Reference to Tests for Hepatic Function, Arch. Int. Med. **44**: 155-193 (Aug.) 1929.
25. Magath, T. B.: The Takata-Ara Test of Liver Function, Am. J. Digest. Dis. & Nutrition **2**: 713-716 (Feb.) 1936.

in the serum is determined by transverse comparison of the serum with standard tubes in a colorimeter. It was recently shown by Magath [25] that the results are extremely satisfactory, since a retention of dye occurred in 96 per cent of cases in which there was evidence of parenchymal hepatic injury or even moderate mechanical obstruction of the bile ducts which had not yet produced clinically demonstrable jaundice. It was observed that low-grade retention of the dye (less than 12 per cent but more than 4 per cent) was significant; indeed, it is most important, for in the presence of such retention clinical judgment is at a low threshold. Occasionally, retention of a low grade does occur without any evidence of hepatic disease, but this is rare. In one series of sixteen cases in which there was retention of the dye grade 1 (from 6 to 12 per cent) there were definite clinical evidences of hepatic injury in thirteen cases.

The test gives results which indicate the extent of parenchymatous damage only roughly but the determinations are sufficiently accurate to yield valuable information if the test is repeated at intervals during the course of the disease. Much confusion has arisen with regard to the interpretation of the results of the tests in cases of jaundice, particularly in those cases in which there is gross mechanical obstruction to the bile passages. While it is true that in most cases of visible jaundice there is complete retention of dye, it does not follow from this that obstruction to the major bile ducts is the only responsible factor. It is more than likely that even transient obstruction causes hepatic cellular injury, but under the circumstances the test cannot reliably indicate the fact. We have seen other cases of visible jaundice in which the test did not reveal significant retention; this is especially true in hemolytic jaundice of the familial type. In resolving jaundice the test frequently furnishes real information as to the progress of the disease, although determination of the values for the serum bilirubin may be superior in this respect. In general, we are not inclined to use the test in cases of clinical icterus, that is, in cases in which the value for the serum bilirubin in more than from 5 to 6 mg. per hundred cubic centimeters, since the element of mechanical obstruction confuses the clinical picture when the values for the serum bilirubin are higher than this. In the absence of jaundice or if the value for the bilirubin does not exceed from 2 to 5 mg. per hundred cubic centimeters, retention of the dye of moderate to maximal degree is important; slight, or grade 1, retention under these circumstances may be discounted to some extent.

In cases in which the patients are not jaundiced and the values for the serum bilirubin are normal, the degree of retention of the dye can be taken at its face value. Positive tests are the rule in chronic atrophy of the liver, cirrhosis, Banti's disease, hemochromatosis, chronic passive congestion, Pick-Concato disease, extensive fatty degeneration of the liver, amyloidosis, chronic hepatitis associated with familial hyperbilirubinemia, and in the recovery state of hepatogenous jaundice. In syphilitic cirrhosis, positive dye tests are the rule; but the degree of retention may be somewhat less than one would anticipate from the clinical evidence of hepatic injury. In these conditions, information of prognostic significance is afforded; high grades of retention of bromsulfalein are indicative of an unfavorable outcome, whereas surgical procedures, such as omentopexy and splenectomy, may be carried out with reasonable safety if dye retention, grade 1 or 2, is present.

The diagnostic value of dye tests in demonstrating a metastatic malignant condition must also be mentioned. Even a relatively moderate hepatic involvement will produce a significant degree of bromsulfalein retention. In many cases of abdominal and rectal malignant conditions observed at the clinic, invasion of the liver has been accurately detected on the basis of the results of this test.

In another group of cases in which toxic or infectious hepatic lesions are presumed to be present the bromsulfalein test will be positive. Among the toxic conditions must be mentioned exophthalmic goiter, a condition which is known to be associated with injury to the liver and poisoning of various types; latent hepatic injury due to cinchophen and other hepatotoxic substances also may be detected in this way. In various infectious diseases, notably undulant fever, retention of bromsulfalein may be noted during the height of the disease. Following an episode of acute cholecystitis or even biliary colic, retention of the dye may also be noted for brief periods. Finally, in the presence of biliary fistula, retention of the dye of high grade is a common finding; its significance is questionable, since in many instances the liver is anatomically normal at operation. Our experience with other dye tests is limited; presumably, the results would roughly parallel those obtained with bromsulfalein.

Among other tests of excretory function of the liver may be mentioned the bilirubin tolerance test. Because of the great value of the determination of the value for the bilirubin in the serum, von Bergmann [26] thought that a further test of the ability of the liver to excrete this substance would be useful. He accordingly devised the bilirubin function test. One milligram of bilirubin per kilogram of body weight is administered intravenously and one then determines whether or not this increases the amount of bilirubin in the serum. The amount of bilirubin present in the serum four hours after this injection is compared with the amount present five minutes after the injection. A retention of more than from 5 to 6 per cent was considered abnormal by Soffer.[1] The test, while theoretically sound, has certain obvious drawbacks, not the least of which is its cost. Soffer reported the results of the test in seventy-two cases of well defined hepatic disease. It was positive in 86.1 per cent of these cases. Since a positive reaction is dependent on an extremely small increase in the amount of bilirubin as compared to the control values, it is evident that the determination must be extremely accurate. Under some conditions the value for the serum bilirubin at the end of four hours may be only 0.05 mg. per hundred cubic centimeters greater than the control value but may represent a retention of 7 per cent. There is of course reasonable doubt that such a small amount of bilirubin may be determined with accuracy. However, the test is said to be extremely sensitive and it no doubt will be improved and adapted to general use. Soffer [1] recently called attention to some important technical modifications and said that the greatest sphere of usefulness of the test is in cases in which the value for the bilirubin does not exceed 1 mg. per hundred cubic centimeters.

MISCELLANEOUS TESTS

The Takata-Ara Test.—This is a colloidal reaction performed on serum; it was first proposed as a method of differentiating bacterial meningitis and syphilitic

26. von Bergmann, G.: Zur funktionellen Pathologie der Leber insbesondere der Alkohol-Aetiologie der Cirrhose, Klin. Wchnschr. 6: 776-780 (April 23) 1927.

involvement of the central nervous system. Jezler [27] later applied the test to the study of parenchymatous diseases of the liver. The literature stresses the importance of the test in identifying cirrhosis of the liver. It is true that in this disease, especially if it is advanced, the test will be positive, but in the earlier stages of the disease many negative tests are obtained. By and large, one may expect to obtain a positive Takata-Ara test in about half of all cases of parenchymatous disease of the liver and there will be a certain group of positive reactions when no evidence can be obtained on which to base the diagnosis of injury of the liver. One may conclude that a positive test does give confirmatory evidence in the diagnosis of cirrhosis, but the results are to be accepted with caution. In the absence of jaundice, this test is certainly not so sensitive as the bromsulfalein test.

The Appearance of Erythrocytes in Disease of the Liver.—This may be mentioned, not as a test of liver function, but because studies on the morphology of the blood may give valuable confirmatory evidence of the presence of injury of the liver. A hypochromic macrocytic anemia is a rather uniform accompaniment of portal cirrhosis and may be noted in other types of injury of the liver. Similar changes have been demonstrated in the experimental animal by Higgins and Stasney.[28] The rapidity with which such macrocytes appear in the blood stream has been explained on the basis of hypoproteinemia and swelling of the erythrocytes because of the altered osmotic pressure of the plasma.

COAGULATION FACTORS; MEASUREMENT OF THE TENDENCY TO BLEED

Many procedures have been designed to measure the coagulation time of the blood accurately, but none give a consistent picture of the dangers of bleeding in hepatic disease. The standard Lee-Vincent method is most generally used, and within the limitations of all such procedures the results are satisfactory. However, patients who have a prolonged coagulation time (in excess of seven minutes) may go through a surgical procedure without difficulty, while in other cases in which the blood appears to clot at a normal rate, fatal bleeding may occur. As Ivy has put it, the best test for bleeding tendencies in disease of the liver is to see whether the patient bleeds. Studies on fibrinogen, on calcium in its diffusible and nondiffusible forms, and on various other constituents of the blood have failed to solve the riddle of why the patient who has hepatic disease is so subject to hemorrhage. The results of recent studies which have been made on recalcified plasma and on whole blood by using physical methods of measurement have been encouraging; Nygaard and Baldes [29] have shown that the "plasma coagulation index," as measured by their method, gives a satisfactory basis for prediction of the tendency to bleed. They also have developed a photo-electric method of observing the coagulation of blood; this method is based on the principle of light extinction by the clot as it forms, which gives a remarkably good idea of the rate of clot formation. Repeated "coagelgrams" will often show the recession or development of the hemorrhagic tendency. Quick and his co-workers [30] have demonstrated a deficiency of prothrombin in cases of jaundice, by a new method of studying the coagulation of blood. The methods which have been mentioned are not as yet in general use and may be too involved for practical purposes; their technical accuracy, however, and their close correlation with clinical observations render them worthy of further study. For clinical purposes, the following rule of thumb can be laid down with regard to bleeding in hepatic disease: (1) Any patient who has an injured liver parenchyma may bleed in spite of normal results of any existing test for coagulating factors; (2) the greater the degree of hepatic insufficiency, the greater the danger of hemorrhage; (3) high values for bilirubin in cases of icterus and high grades of retention of bromsulphalein in cases in which there is no icterus are danger signals and furnish information which is as reliable as that furnished by any current method of studying coagulation of blood.

THE ELIMINATION OF BILE SALTS

The salts of cholic acids, as they are found in bile, represent an exclusively hepatic product. As Smyth and Whipple [31] demonstrated years ago, the rate of their production in a dog which had a biliary fistula seemed to reflect the functional state of the liver; after the administration of hepatotoxic substances the concentration and total output of bile acids fell to very low levels and rose as recovery took place. Naturally, many attempts have been made to study the production of bile acids in the human subject, as a test for liver function. Determination of the amount of bile acids in duodenal contents, while entirely possible, is of little value since the material studied is a mixture of bile and secretions from the digestive tract. No known method of determining the amount of bile acids in the blood is satisfactory; this closes a promising method of approach. The determination of the amount of bile acids in the urine is subject to too many variable factors to make it a matter of clinical importance in cases of jaundice. Following operation, when bile can be obtained from drainage tubes or from fistulas, the study of bile acids by using the Gregory-Pascoe method of determination may give useful information, as numerous investigations have shown that low concentrations consistently are of grave prognostic significance. While there is usually a period after operation when the concentration and total output of bile acids are decreased, ordinarily normal values are attained within a few days, when and if the liver regains its normal capacity to manufacture these substances. Further simplification of the method will undoubtedly make it available for more general use; even now it is clear that much may be learned from the study of bile obtained from fistulas either before or after operation.

QUANTITATIVE ESTIMATION OF PHOSPHATASE

Phosphatase, which is an enzyme concerned in the metabolism of bone, is present in many tissues of the body and is found in high concentrations in bone, kidney, intestinal mucosa and liver. Roberts [32] first noted that high values for phosphatase in the serum were a feature of some cases of obstructive jaundice, while,

27. Jezler, Adolf: Die Takatasche Kolloidreaktion in Serum und Körperflüssigkeiten und ihre Beziehungen zu Störungen des Eiweissstoffwechsels der Leber, Ztschr. f. klin. Med. **114**: 739-756, 1930.
28. Higgins, G. M., and Stasney, Joseph: Macrocytic Anemia in Experimental Cirrhosis, Proc. Staff Meet., Mayo Clin. **10**: 429-432 (July 3) 1935.
29. Nygaard, K. K., and Baldes, E. J.: Interpretation and Clinical Significance of Coagelgrams in Obstructive Jaundice, Proc. Staff Meet., Mayo Clin. **11**: 705-709 (Nov. 4) 1936.
30. Quick, A. J.; Stanley-Brown, Margaret, and Bancroft, F. W.: A Study of the Coagulation Defect in Hemophilia and in Jaundice, Am. J. M. Sc. **190**: 501-511 (Oct.) 1935.
31. Smyth, F. S., and Whipple, G. H.: Bile Salt Metabolism: I. Influence of Chloroform and Phosphorus on Bile Fistula Dogs, J. Biol. Chem. **59**: 623-636 (April) 1924.
32. Roberts, W. M.: Variations in the Phosphatase Activity of the Blood in Disease, Brit. J. Exper. Path. **11**: 90-95 (April) 1930.

in the nonobstructive types, low or normal values were the rule. A considerable number of papers lately have appeared on this subject, most of which have been cited in a recent article by Rothman and his collaborators.[33] The technic generally used in the determination is that of Roberts; this involves a determination of inorganic phosphate liberated when the enzyme present in the blood is allowed to act on a phosphoric acid ester substrate under standard conditions. The upper normal value for adults is approximately 6 units and that for children is 15 units. Rothman and his collaborators [33] recently stated that in most cases of proved obstructive jaundice the value for the phosphatase was more than 10 units but that values of 20 or more units were commonly observed; in cases of nonobstructive jaundice values of less than 10 units were the rule. Our own experience with the method has not been large but in general the results have been in agreement with Rothman's. Greene and his collaborators,[34] on the other hand, expressed the opinion that the information obtained by determinations of phosphatase is inaccurate and does not differentiate the type of jaundice in question. Further experience will be required to establish the proper place of this test, but it is apparent that the results of the determination of phosphatase will have to be weighed against the clinical evidence in cases in which the diagnosis is doubtful.

TESTS OF THE DETOXIFYING FUNCTION OF THE LIVER (SYNTHESIS OF HIPPURIC ACID)

The ability of the liver to remove from the circulation various noxious substances, alter them chemically, or combine them with certain common constituents of blood in such a manner as to render them physiologically inert has been known to physiologists for years. The conversion of indole to indoxyl sulfuric acid, the conjugation of cholic acid to form bile salts, and the formation of conjugated glycuronates are familiar examples of this process. Various clinical tests with such substances as thymol, menthol, camphor, salicylates, phenol and *p*-cresol, and guaiacol sulfuric acid have been used but have not been entirely successful. The only survivor of such tests of the detoxifying function is one that is based on the ability of the liver to conjugate benzoic acid and aminoacetic acid to form hippuric acid. Early studies by Bryan [35] and more recent application of the test by Quick [36] have shown that the results are consistent in hepatic disease. While the early studies of Bunge and Schmiedeberg [37] showed that in the dog the synthesis of hippuric acid is affected by the kidney, this is probably not the case in the human being and, as Quick [36] has pointed out, the results seem to depend largely on the rate at which the liver can supply aminoacetic acid. It has been reasonably well established that, if the value for the blood urea is normal, the rate of synthesis of hippuric acid in clinical patients can be correlated with the degree of hepatic injury.

The test is performed by administering 6 Gm. of benzoic acid to the fasting patient and collecting the urine for four hours thereafter. A simple gravimetric method of analysis is used in determining the amount of hippuric acid; a correction is made for the hippuric acid still dissolved in the urine and the result converted to terms of benzoic acid by multiplying by the factor 0.68. For normal persons the excretion of hippuric acid (calculated as benzoic acid) ranges from 2.6 to 3.3 Gm.; to exclude a possible factor of delayed elimination by the kidney, Kohlstaedt and Helmer [38] suggested making a simultaneous study of urea clearance. If this can be done, reduction of synthesis of benzoic acid to less than 2 Gm. may probably be regarded as significant. In a large number of these tests performed at the clinic in the past two years, it has been noted that for patients who are not jaundiced the results closely paralleled the more familiar bromsulfalein test, while in cases of hepatogenous or obstructive jaundice the reduction in the synthesis of hippuric acid corresponded in a general way to the degree of hepatic injury noted at operation or necropsy. In "surgical" types of icterus it was found that values of less than 1.5 Gm. were associated with an unfavorable prognosis and that few patients survived if this or a greater degree of hepatic insufficiency was indicated by the test. The simplicity of the test, its adaptability to the jaundiced patient, and its apparent reliability recommend it for general use, particularly in evaluating prognosis and surgical risk. Some care must be taken to eliminate the factor of renal injury, which may influence the result; dehydration and malnutrition likewise seem to depress the possible rate of synthesis. Gastric retention must obviously be considered as a possible explanation in cases in which low values cannot be otherwise explained.

SUMMARY AND CONCLUSIONS

In the foregoing paragraphs we have reviewed the theoretical basis, methods, limitations and interpretations of a series of tests for liver function in use at the Mayo Clinic. It has been emphasized that many of the procedures are not functional tests at all but merely laboratory procedures which throw some light on one or another aspect of disease of the liver. We have attempted to outline the particular field of usefulness for each of the tests and to point out that none of them are infallible or universally applicable. For practical purposes it may be said: (1) In types of disease of the liver not associated with jaundice, information gained from the study of retention of bromsulfalein is as reliable as that which can be gained in any other way, and that under these conditions other tests give chiefly confirmatory evidence; (2) in cases of jaundice, some information, which is not altogether reliable, as to the possible hepatogenous or obstructive nature of the jaundice in any given case can be had by studies on excretion of galactose, the value for cholesterol and cholesterol esters in the plasma, and the value for serum phosphatase, and (3) the best information as to the state of functional activity of the liver in cases of jaundice can be gained from a consideration of the value for the serum bilirubin, its daily variations and a knowledge of the anatomic changes which these may represent. So far as indirect methods of measuring liver function in the presence of icterus are concerned, the hippuric acid test gives reasonably accurate results, which should not, however, supplant the impressions gained from purely clinical study.

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ROCKY MOUNTAIN SPOTTED FEVER IN THE EAST

REPORT OF A CASE

LAWRENCE S. CAREY, M.D.

Physician to and Chief of the Medical Outpatient Clinic, Pennsylvania Hospital; Demonstrator of Medicine, Jefferson Medical College

AND

GARFIELD G. DUNCAN, M.D., C.M. (McG.)

Chief of Medical Service B, Pennsylvania Hospital; Assistant Professor of Medicine, Jefferson Medical College

PHILADELPHIA

Statistics from the public health department[1] given in the accompanying table show that prior to the positive identification of Rocky Mountain spotted fever in the East by Badger, Dyer and Rumreich[2] in 1931 only three cases had been reported east of the Mississippi River, one in Indiana (1925), one in New York (1925) and one in Norfolk, Va. (1926). The frequency of recognition of the disease in the Eastern states has steadily increased, however, in the last decade. We know of eight cases in the region of Philadelphia in the last two years, and an outbreak occurred in southern New Jersey in the spring of 1937. This continued recurrence of the disease in our vicinity, as well as reports from other eastern localities, has impressed us with the fact that the disease is established permanently in the East. Some authorities[3] have stated that the disease has been present in the East for a very long time but that it has only recently been recognized. This fact and the report of a case of Rocky Mountain spotted fever contracted in southern New Jersey and admitted to the Pennsylvania Hospital in June 1936 is therefore a timely reminder to be on the lookout for the disease.

Spotted fever is conveyed to man from infected animals by the tick.[4] The chief vector of the Western, or Bitter Root Valley, type is the wood tick (Dermacentor andersoni), whereas in the East it is the dog tick (Dermacentor variabilis). Many animals, both domestic and wild, particularly of the rodent family, act as hosts for the transmission of the disease from tick to tick. Moreover, eggs, larvae and nymphs[5] which have never fed on any infected host have been shown to contain Rickettsial bodies, proving that the disease in ticks may be hereditary. The rabbit tick transmits the disease from rabbit to rabbit[6] but has never been known to transmit the disease directly to man. However, if the infected rabbit becomes host to a dog tick, the dog tick may transmit a more severe form of the disease to man. Passage of the virus through the wood tick or dog tick seems to enhance its virulence.[2] Certain birds, notably the meadow lark, and mice have been shown recently to be possible carriers.[6]

In man the incubation period of the disease is from two to twelve days, with prodromal backache, malaise and anorexia. The onset is characterized by chills, fever and headache, and on about the second to the fourth day a petechial rash appears on the wrists, forearms and ankles, gradually spreading to the back, arms, legs and chest. The palms of the hands and the soles of the feet are commonly involved, the face rarely. The rash, at first petechial, becomes macular and more confluent as the disease progresses. The fever reaches its height during the second week and falls, usually by lysis, after from twelve to twenty-two days. Stupor and delirium may be prominent features.

Pathologically,[7] the disease primarily affects the blood vessels. Panangeitis with thrombonecrosis is the specific lesion, as contrasted to the proliferative panangeitis of typhus. Enlargement of the spleen, bronchopneumonia and meningeal congestion are prominent in the Eastern, whereas scrotal gangrene and serous ecchymosis are more prevalent in the Western, type.

The mortality in the East has been estimated to be about 25 per cent,[8] whereas in the Bitter Root Valley (Montana) it has reached from 80 to 90 per cent. The disease seems to be less severe in younger persons.

The clinical features readily differentiate the disease from most other exanthems. Meningitis may at first be suspected but normal spinal fluid readings readily exclude it. The positive Weil-Felix test, i. e., agglutination of Bacillus proteus X 19 or X 2, which is obtained usually within a week of the onset of the disease, definitely places it among the Rickettsial

*Number of Cases of Rocky Mountain Spotted Fever Reported in the United States for the Years 1925-1935, Inclusive (U. S. Public Health Service)**

State	1935	1934	1933	1932	1931	1930	1929	1928	1927	1926	1925
Middle Atlantic											
New York	4+	4	3	..	..	..	..	..	..	..	..
New Jersey	1	..	..	3	1	..	..	..	..	..	..
Pennsylvania	3	1	2	..	1	..	..	..	..	..	..
East North Central											
Indiana	..	..	1	..	..	..	..	..	..	..	..
Illinois	2	1	..	..	..	..	..	..	..	..	..
West North Central											
Minnesota	1	..	1	..	1	..	..	..	..	..	..
Iowa	7	6	5	..	..	..	..	..	..	..	..
North Dakota	2	..	..	..	..	..	..	..	..	1	..
South Dakota	11	5	2	13	1	..	..	..	..	3	2
Nebraska	1	..	..	..	..	..	..	..	..	..	..
Kansas	..	..	..	..	1	..	..	..	..	..	1
South Atlantic											
Delaware	..	3	..	..	1	..	..	..	..	..	..
Maryland	33	33	55	49	38	..	..	..	..	..	..
District of Columbia	6	4	7	9	11	..	..	..	..	..	..
Virginia	44	47	23	29	22	..	..	..	..	..	..
West Virginia	5	..	..	..	..	..	..	..	..	..	..
North Carolina	21	34	27	7	8	..	..	..	..	..	..
South Carolina	2	1+	..	6	5	..	..	..	..	..	..
Georgia	..	1	3	..	..	..	..	..	..	..	..
Florida	..	2	..	..	..	..	..	..	..	..	..
East South Central											
Kentucky	..	2	..	..	..	..	..	..	..	..	..
Tennessee	1	3	2	1	4	1+	..	..	..	..	..
Alabama	3	1	2+	..	..	..	..	..	..	..	..
West South Central											
Louisiana	..	..	..	..	5	..	..	..	..	..	..
Oklahoma	..	..	..	..	..	..	1	..	..	..	..
Mountain											
Montana	126	74	67	100	30	20	20	32	37	36	33
Idaho	28	35	47	27	20	20	55	17	23	29	17+
Wyoming	95	95	118	82	26	41	66	66	106	90	28
Colorado	21	5	14	15	6	17	13	10	9	2	2
New Mexico	..	..	..	2	..	..	2	..	1	..	..
Arizona	..	..	..	1	1	..	..	..	..	..	..
Utah	14	12	5	..	10	13	11	..	..	..	6
Nevada	5	5	15	14	18	15	30	14	7	..	9
Pacific											
Washington	3	9	3	1	..	2	5	2	2	1	1
Oregon	40	58	50	55	52	62	74	26	26	30	18
California	10	16	16	7	1	7	13	8	2	3	3

* Spaces in which numbers do not appear indicate that no cases of Rocky Mountain spotted fever were reported. States omitted did not report any cases of Rocky Mountain spotted fever.

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diseases.[9] Pinkerton[10] of Harvard has laid down in detail the criteria which enables the differentiation of Rocky Mountain spotted fever from the other members of this group.

Numerous widespread diseases fall into the Rickettsial group, four of which are immunologically distinct:[11] typhus, tsutsugamushi, spotted fever and trench fever. Of the eleven classified by Dyer,[11] typhus, spotted fever and tsutsugamushi predominate. The other members of the group are (1) South African tick fever, (2) pseudotyphus of Sumatra, (3) tick typhus of India, (4) a typhus-like disease in Australia, (5) tropical typhus of the Malay states, (6) rural typhus-like disease in Kenya East Africa, (7) fièvre boutonneuse of the Mediterranean Littoral and (8) exanthematic typhus of São Paulo, Brazil.[12] Dyer did not include trench fever in this classification. Fièvre boutonneuse and exanthematic typhus of São Paulo have been shown by Davis and Parker[13] to be immunologically the same as spotted fever. Perhaps others of this group will ultimately be classifiable immunologically as either typhus, tsutsugamushi or spotted fever.

Typhus, so far as is known, is the oldest of the recognized Rickettsial diseases. It is a lice and flea borne disease. It is therefore chiefly urban in distribution and is more common in the fall and winter months. The rash of typhus occurs first on the body and, unless the attack is severe, does not spread to the face and extremities.

Tsutsugamushi, also of this group, has not been reported in this country. It has quite distinct clinical features; it is endemic in Indo-China and is disseminated by mites.

Trench fever, particularly prevalent during the World War, is disseminated by the body louse and runs a short course (from one to five days).

Spotted fever is next to typhus in importance. The history of tick contact is often obtained. The disease is rural and occurs in the tick season; i. e., during the spring and summer months. The rash begins on the extremities and extends to the body. The final differentiation between typhus and spotted fever rests on cross immunity or neutralization tests in animals.[14] The latter is done by mixing convalescent serum with the known virus and inoculating a guinea pig with the mixture. If no disease results, the virus used indicates the strain. The cross immunity test consists of the inoculation of animals recovered from known strains with blood from the patient. If no disease results in the animal, the disease in question is the same as that from which the animal recovered.

The prevention of spotted fever consists chiefly in measures directed against ticks. In regions in which ticks are prevalent a careful search for ticks on the body at least twice a day is an important precaution. The virus is not transmitted for several hours after the tick begins to feed,[15] probably because the dormant virus in the tick becomes activated by fresh blood. The wearing of suitable clothing with the upper garment stuffed into the lower, because the ticks always crawl upward before becoming attached, is helpful. The immersion of domestic animals in arsenic trioxide solution (sodium carbonate 24 pounds, arsenic trioxide 8 pounds, pine tar from 1 to 2 gallons, water 500 gallons), and the presence of chickens, which eat ticks and are immune to the disease, are also helpful measures. The establishment of tick parasites in tick-infested areas is also worth while.

A vaccine prepared by grinding up infected ticks in a phenolized emulsion and using the supernatant fluid is a useful prophylactic agent and should be used in regions where the disease is prevalent. This vaccine is given in two subcutaneous injections of 2 cc. each for adults and 1 cc. each for children under 10 years of age.

REPORT OF CASE

M. P., a youth, aged 16, admitted to the Pennsylvania Hospital July 2, 1936, complained of headache, nausea, vomiting, fever and "chilly sensations" dating from June 26. A skin rash and photophobia were among the complaints. Past illnesses and the family history were not important.

The boy had left Philadelphia June 14 to pick berries at Blue Anchor, N. J., where he drank water from a spring and went swimming in a fresh water lake. He gave a history of picking ticks from a dog and crushing them with his fingers but did not recall being bitten.

June 26 he suffered from headache and nausea; he became feverish June 28; anorexia and general weakness followed. June 29 he had epistaxis followed by expectoration of blood-stained sputum and he vomited all nourishment that he took. He was given an enema twice because of constipation.

Because of continued fever with delirium and the appearance of a rash the patient was brought to his home in Philadelphia. According to the patient's brother the rash appeared first on his chest, spreading to his arms, but after recovery the patient recalled that the rash began on his extremities and involved the body later.

On admission July 2 he was seriously ill, with a temperature of 104 F., pulse 100, respiration rate 32. He was very weak, apathetic, sluggish and confused. A foul and sweetish odor on the breath was noted. He was slightly, and later markedly, hyperesthetic, resenting examination or handling. There was a maculopapular rash distributed profusely over the trunk, buttocks, median aspect of the arms, palms of the hands, dorsum and soles of the feet. The pinkish papules were slightly raised and varied in size from minute specks to 2 or 3 mm. in diameter. Some faded on pressure but most of them did not. These spots later, July 4, became a dull purple, giving a splotchy appearance.

The other positive manifestations were blood pressure 100 systolic, 70 diastolic; bloody crusts about the nose, conjunctivae injected, pupils dilated, lips dry, tongue slightly coated and pharynx mildly injected. Flexion of the neck caused pain. The reflexes were normal but the patient winced when tapped lightly with a percussion hammer.

July 3 he was seen by one of us (G. G. D.) and the following additional notes were made: The cheeks were heavily tanned and flushed; the tongue was coated; there was some reddening of the uvula and pharynx; the submaxillary glands were enlarged and tender on the left side; there was no rash on the face. The rash over the body and arms was papulomacular, the isolated eruption being pinpoint to pinhead in size, not palpable, and most of them blanched on pressure; there was tenderness in the left axilla on pressure, roughening of the first sound at the cardiac apex; distant aortic first with accentuated aortic second sound; the abdomen was slightly distended, with slight tenderness in the upper part; spleen was not palpable; tenderness about the knees, tibias and muscles in general was noted.

July 4 the temperature was still between 103 and 104 F. The rash did not fade on pressure and had become dull purplish.

July 5 the patient was very stuporous, mumbled to himself, was irrational, cried out in sleep and had incontinence of urine.

July 7 there was severe epistaxis and he complained of headache.

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July 8 the temperature dropped from 102.3 to 97 F. at 3 p. m.; the patient was clearer mentally.

July 9 the temperature was elevated, to 102 F. The mental reaction was clearer.

July 10 there was severe epistaxis; stupor was less marked.

July 20 the rash was about gone except for slight pigmentation. Constipation was troublesome; the temperature and pulse had been normal since July 16.

July 22 the skin was desquamating in branny flakes with small scales on the hands and feet but none on the face.

July 25 the patient was allowed up. The convalescence was uneventful.

During the acute phase the body temperature oscillated between 102 and 104 F. It dropped to normal for two readings on July 8 but on July 9 and 10 it resumed its former level. A fall by lysis followed.

Additional Data.—Blood: there was a leukocytosis of from 16,000 to 22,000 with a mild secondary anemia. July 13 the agglutination test with Proteus X 19 was positive in 1:160 concentration and on July 24 it had risen to 1:1,280.

The blood Wassermann reaction was negative. The blood culture, spinal fluid, stool and urine were normal.

The diagnosis of spotted fever was confirmed by a positive neutralization test done through the courtesy of Dr. R. E. Dyer of the Public Health Service of Washington, D. C.

The treatment was identical with that of typhoid, consisting of isolation, rest in bed, tepid sponging, acetylsalicylic acid for headaches and phenobarbital for insomnia; liquid diet, high in calories and given at frequent intervals.

1930 Chestnut Street.

FILTRABLE VIRUSES IN INFECTION OF THE UPPER RESPIRATORY TRACT

A. R. DOCHEZ, M.D.
KATHERINE C. MILLS
AND
YALE KNEELAND JR., M.D.
NEW YORK

In the past ten years a considerable amount of knowledge has accumulated relating to the etiology and the mechanism of infection of the upper respiratory tract. Beginning with the common cold, it has been shown that there exists in this disease a filtrable virus [1] which can readily be demonstrated in the secretions of the upper respiratory tract. The evidence for the existence of this virus rests on numerous transmission experiments in which typical acute colds have been produced under conditions of strict quarantine, both in anthropoid apes and in human volunteers, by intranasal inoculation of material derived originally from a human being with an early cold and freed from associated bacteria by filtration. The regularity with which this filtrable virus can be recovered from patients with colds and the failure to demonstrate it in the secretions of normal persons have led to the belief that its role is one of etiologic importance. The precise extent of this importance, however, is as yet hard to define. Studies [2] of isolated communities suggest powerfully, although they do not conclusively prove, that without the virus the whole complex of infection of the upper respiratory tract ceases to exist; i. e., that the bacteria of the upper respiratory tract are of themselves powerless to initiate infection. If this is true, then the virus can be regarded as the primary etiologic agent of infection in the upper respiratory tract. Once the infection is started, pathogenic bacteria undoubtedly can play a role in influencing its severity and producing complications. There exists some evidence on the mechanism of this interaction between virus and bacteria—evidence that, in addition to "activating" the bacteria,[3] the virus may assist in their dissemination [4] and even increase their essential virulence.[5]

Considerations such as these have emphasized the importance of the virus component in infection of the upper respiratory tract, and it seemed to us desirable to make an extensive study of the general biologic properties of the cold virus. Our first experiments of this nature dealt with its survival. It was found that relatively short exposure to a temperature of 56 C. completely inactivated the virus. We next showed that it could be preserved at ice box temperature if anaerobic conditions were maintained; i. e., that the original filtered nasal washing would retain full activity for at least a fortnight if stored in the cold under a petrolatum seal with cysteine hydrochloride. Later on we demonstrated that if the original filtrate was frozen rapidly and desiccated in a high vacuum it would remain fully active for at least four months. It was also found that the cold virus could be passed from one person to another; although the virus retained its activity we were unable to demonstrate any enhancement of virulence by such a procedure.

Our next efforts were directed at cultivating the virus in an artificial medium. For this purpose we employed a modification of the technic of Li and Rivers, in which a small amount of minced living chick embryo tissue was incorporated in a fluid menstruum; as we had already shown that the virus survived under anaerobic conditions, this medium was modified to secure anaerobiosis, and by this means the multiplication of the cold virus in vitro was demonstrated in seven of eight attempts at the initiation of a culture. Prolonged experience in cultivating the cold virus has indicated that strains transferred at intervals of two or three days maintain their virulence better than strains transferred after longer incubation. By this method fully active virus has been demonstrated in the eighty-eighth transfer of a culture seven months after the original isolation of the virus from its human source. We invariably found, however, that a falling off in virulence occurs if strains of virus are cultivated for much longer periods than this. Attempts at cultivating the cold virus under aerobic conditions have been unsuccessful.

When the tissue culture medium containing virus is removed from the incubator and kept on ice, it has been found that a rapid inactivation of the virus takes place, presumably due to the injurious effect on the virus of products of the disintegrating tissue. The same inactivation occurs even if the material is frozen and dried immediately after incubation. However, if a small quantity of acacia [6] is added on removal from the incubator before freezing and drying, then the virus will remain fully active for a considerable period. A

From the Department of Medicine, College of Physicians and Surgeons, Columbia University and the Presbyterian Hospital.

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method therefore is available for the production and preservation of cold virus in unlimited amounts.

In addition to the use of the tissue medium described, we have recently employed the chorioallantoic membrane of the developing chick embryo as another means of cultivating cold virus. This technic has been used in connection with a number of filtrable viruses.[7] In our experiment[8] the chorioallantoic membranes of developing embryos were inoculated with a small amount of filtered nasal washings immediately after their isolation from a patient with an acute cold. Incubation was allowed to continue for two or three days, and then the ground up membranes were used for passage to the next series of eggs. Membranes from the third series of eggs were used for testing on two human volunteers, in both of whom typical acute colds developed. It appears therefore that cold virus can be cultivated in the developing chick embryo directly after isolation from its human source.

In summary, then, it has been demonstrated by a large series of transmission experiments on human beings that there exists in the common cold a filtrable virus which in all probability is the primary etiologic agent and can interact with the various pathogenic agents of the upper respiratory tract to produce more severe infections. The evidence, however, from numerous bacteriologic observations during transmission experiments is to the effect that the uncomplicated cold in adults is practically a pure virus disease. Certain of the biologic properties of this virus have been investigated, and a method has been developed for its artificial cultivation and preservation.

It was logical to apply the technic used in investigating colds to the problem of influenza. Influenza is a disease in the study of which one is faced at the outset with a difficulty of definition. In the first place, there is an obvious clinical difference between the severe manifestations of the 1918 pandemic and the milder manifestations seen in the small outbreaks of recent years. In the second place, it is difficult to make a satisfactory clinical diagnosis in an isolated case, with a resulting tendency for the physician to make a diagnosis of influenza in cases of sinusitis, streptococcic infection of the throat, gastroenteritis and, in fact, any febrile disorder in which the cause is uncertain. The great volume of research during and immediately after 1918 concerned itself chiefly with the bacillus of Pfeiffer (Haemophilus influenzae), as well as with one or two other organisms, and an enormous mass of contradictory evidence and opinion was recorded. Experiments at that time designed to test for the presence of a filtrable virus of influenza were few in number, limited in scope and also contradictory in outcome.[9] More recently, in 1931, Long and his co-workers[10] reported transmission experiments on chimpanzees suggesting the presence of a filtrable virus in influenza. However, the next year Costa Mandry and his associates[11] failed in an attempt to transmit influenza to human beings by means of filtered throat washings.

Our own studies of influenza were made with material derived from patients who had the disease in 1931, 1932, 1933, 1934 and 1935 in the winter months, when mild influenza of the interpandemic variety was prevalent. Our criteria for the diagnosis of influenza were as follows: The patient must show a sudden onset with a history of previous freedom from infection; constitutional symptoms must dominate the symptoms of local irritation of the upper respiratory tract; fever must be present and leukocytosis absent. Making use of these criteria, we obtained material from one patient in each of the five years mentioned. In the first year transmission to human volunteers was done with a filtered nasal washing directly after its being obtained from the patient; in the subsequent years the material was cultivated in anaerobic tissue medium and tested after many transfers in vitro.

Our experiences with influenza, which have been described elsewhere in detail,[12] may be summarized as follows: a total of thirty-nine tests on human volunteers has been made under conditions of strict quarantine with the five materials mentioned; with four of these a virus was demonstrated which, although productive of some constitutional reaction, could not be distinguished with certainty from the virus of the common cold. The fifth virus, obtained originally in a small but clinically severe outbreak, did produce in one of several volunteers an acute febrile disorder resembling influenza. The most that it was possible to conclude from this limited number of experiments was that a filtrable virus had been recovered from patients with interpandemic influenza.

The problem of influenza, however, was approached in 1933 by another technic. In England, Smith, Andrewes and Laidlaw[13] reported the isolation of a filtrable virus from a patient with influenza which produced a febrile catarrhal disorder when introduced into the nasal passages of ferrets. This observation was soon confirmed by Francis,[14] in this country. Since that time a great deal of important research has been carried out with human influenza virus both in England and in this country by the investigators mentioned.[15] The results of this research may be summarized as follows: Several strains of the virus which is pathogenic for ferrets have been obtained, and they have been obtained exclusively from patients with typical attacks occurring in fairly severe outbreaks of the disease. Once established in ferrets the disease can be transmitted to white mice, in which after a few passages it produces a fatal pneumonia. Protective substances against this virus are found in the serum of ferrets recovered from the disease and also in the serum of human convalescents, as well as in many normal human serums. The production of antiviral substances in the serum can also be artificially effected by injecting virus into such unsusceptible animals as the rabbit and the horse. Immunologic studies performed with these various serums indicate that strains of influenza virus from different parts of the world are similar. Lastly, the virus can be cultivated in fluid medium con-

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taining minced chick embryo tissue under aerobic conditions, and it has also been shown to propagate in the chorioallantoic membrane of the developing chick embryo.

On the other hand, attempts to initiate a transmissible virus disease in ferrets with material derived from persons with common colds or, for that matter, from persons with any condition except typical influenza in fairly severe outbreaks have been failures. An evaluation of all these results can therefore be made as follows: The primary etiologic agents of certain acute infections of the upper respiratory tract seem to be filtrable viruses; the fact that virus from patients with severe influenza is pathogenic for ferrets and can be cultivated best in aerobic medium while virus from patients with colds or related infections is not pathogenic for ferrets and has been cultivated only under anaerobic conditions suggests that there exist at least two different types of filtrable virus—the cold virus and the virus of epidemic influenza. Until recently the failure to adapt cold virus to small laboratory animals has prevented any immunologic proof of such a dissimilarity. However, in the past year we succeeded in establishing a disease in mice by intranasal inoculation of cold virus growing in the chorioallantoic membrane of the chick embryo. This disease was characterized by areas of pulmonary consolidation and was fairly readily transmissible in series, although it did not carry so high a mortality rate as disease due to influenza virus in mice. Preliminary studies [16] with immune serums were apparently showing an immunologic dissimilarity between cold virus and influenza virus when the course of the experiments was interrupted by the appearance of a new and highly fatal virus which became mingled with all the strains of cold virus and abruptly terminated the experiments. This new virus was found later to be present occasionally in the lungs of apparently normal mice and to undergo a rapid enhancement of virulence on repeated intranasal passage, a fact which makes great caution necessary in interpreting results obtained with such a technic.

The objective of all this work, naturally enough, has been the development of some satisfactory means of prophylaxis against infection of the upper respiratory tract in human beings. Our hope has been stimulated by the successful vaccination of certain animals against virus infections such as canine distemper and, more especially, swine influenza. The latter disease furnishes somewhat of an analogy to infection of the upper respiratory tract in human beings, for it has been clearly shown by Shope [17] to result from the combined activity of a filtrable virus and a bacterium, Haemophilus influenzae suis, resembling the bacillus of Pfeiffer in man. Although this bacterium is necessary to produce the full clinical severity of the disease, it is powerless to initiate it, and Shope discovered that a solid active immunity could be generated in swine by parenteral injection of living virus alone. Believing as we did that the cold virus was similarly the agent of primary etiologic importance in human colds, we hoped to be able to create an active immunity in man by the same method. Having developed a technic for the production and preservation of cold virus which rendered it available at all times and in a condition of proved bacteriologic sterility, we were in a position to attempt such an experiment. After a preliminary trial with chimpanzees, which yielded encouraging evidences of active immunity, several groups of human beings were given subcutaneous injections of living virus. Careful study of their subsequent clinical histories failed to reveal any real evidence that protection against colds had been developed by this means. The explanation of this negative result cannot yet be made—whether it is due to the existence of a multiplicity of strains of virus, to the impossibility of preparing virus in large quantities free from the constituents of the nutrient medium or to the possibility that resistance to colds is a purely local rather than a general bodily phenomenon. In any case, these early attempts must be regarded as failures, although this does not prove that with some future modification of technic the enterprise may not be successful.

With regard to the prophylaxis of influenza, the situation may be regarded as more encouraging. Francis and Magill [18] have reported the production of immune substances in the serum of persons vaccinated with a mouse passage strain of influenza virus cultivated in tissue medium. More recently Stokes and his associates [19] have described what appears to be active immunity in a group of persons similarly treated.

The foregoing is a brief summary of researches which have been carried out in several laboratories during the past decade, and it is obvious that the problems studied are as yet remote from practical solution. Nevertheless, it seems fair to assert in conclusion that a certain amount of progress has been made—that light has been shed on complex mechanisms and that methods have been developed which may have future value.

620 West One Hundred and Sixty-Eighth Street.

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ABSTRACT OF DISCUSSION

DR. RUSSELL L. CECIL, New York: To a practitioner the respiratory infections are of intense interest because they make up such a large part of practice. One of the most interesting phases is "virus pneumonia" which occurs in ferrets and mice and which usually is not associated with any secondary infection with pathogenic cocci. It leads one to speculate as to just how often in severe, fulminating influenza in man there exists first a virus pneumonia before the secondary invaders make their appearance. I have not seen at autopsy a virus pneumonia in man, but that might be explained in various ways. When one sees influenza virus pneumonia in the ferret, one wonders whether in 1918 a great deal of the pneumonia was not primarily a virus pneumonia, with bacillus influenzae, streptococcus, and pneumococcus acting as secondary invaders. Practitioners know but little about the technical side of viruses but are tremendously interested in any efforts toward vaccination with viruses and regret to hear from Dr. Dochez and his co-workers that first experiences with cold virus vaccine have been disappointing. I feel as they do that the question is just beginning to be studied and that much more work will have to be done before the possibilities of an effective cold virus vaccine can be dismissed. The old coccus vaccines which many take in wintertime in the hope that they will give some protection are not entirely without benefit. For many years I have used these vaccines, as made up by the commercial houses, and occasionally autogenous vaccine, and it is surprising how in some people they give definite protection. The authors' work showed that while the ordinary coccus vaccine did not give protection in young children it gave them a milder type of cold. The colds were less severe and less frequently followed by complications such as otitis, mastoiditis and pneumonia. It may be found that, by combining a virus vaccine with a coccus vaccine, better results will be obtained than with either of these vaccines alone. Dr. Francis Blake and I, during the war, swabbed the noses and throats of monkeys with freshly

isolated Pfeiffer bacilli. They got a respiratory infection and they got it without any preliminary virus infection. It was not, however, a perfect imitation of influenza in man. It was not so severe, though one or two monkeys got secondary pneumonia and pansinusitis. Dr. Blake and I were misled at that time into believing that the influenza bacillus was probably the cause of the pandemic. The work on viruses has shown that we were wrong in that contention. It is rare to see either rheumatic fever or acute arthritic infections without a preceding respiratory infection, and it looks as though the hemolytic streptococcus was the organism usually implicated in these cases. There is the cycle of influenza attack, secondary invasion with hemolytic streptococci and finally the metastatic or allergic manifestations in the joints.

DR. L. D. BRISTOL, New York: In the Bell Telephone System during the last fifteen or twenty years about 20,000 employees, largely through the cooperation of their family physicians, have been given the so-called cold vaccines. Our experience has been that they haven't prevented colds but that they have definitely cut down length of disability in many instances, and that in industry is a primary objective.

DR. HENRY F. VAUGHAN, Detroit: There is little I can add to what Dr. Cecil has said. I might refer to the fact that in the outbreak at Camp Wheeler there was an epidemic of type I pneumonia quite specific in type, which preceded the inoculation with the specific types I, II and III pneumococcus vaccine. Following that outbreak of pneumonia, which included a series of ninety deaths (the results have never been published but they are a matter of record in the Surgeon General's Office), there was no more pneumonia of that type. What impressed us especially was the widespread, numerous type I pneumonias. That was as fulminating an epidemic as I have ever seen, influenza, smallpox or any other communicable disease, but after the vaccination had been performed on the raw troops and those already in the camp there was no more pneumonia of that type, but on top of that came the complication of the epidemic of influenza, and the armistice came too soon to complete the work. We have often wished the armistice had been delayed slightly, so that we could have accomplished more work.

DR. M. L. BLATT, Chicago: I am wondering, after listening to the admirable discussion of Dr. Dochez and his co-authors, whether they might not have had better results in protection against the common cold if this infection were as accurately defined as influenza is defined. Many who practice pediatrics find other diseases diagnosed as a common cold. Cases so diagnosed are food, pollen or bacterial allergies. Some are old sinus infections which recur and a number are of the so-called histamine type, a rhinorrhea brought on by drafts or exposure. One of the greatest difficulties in the careful evaluation of virus vaccination against the common cold will result from the difficulty in diagnosis. With influenza, however, the picture is quite different. It is a recognized entity. It is not confused with streptococcic nose or throat infections. Influenza is a three day infection, easily diagnosed in the presence of an epidemic and usually when endemic if white blood counts are made. With regard to the coccus vaccines in childhood, I have had good results from the use of lysed coccal vaccines at the St. Vincent's Orphanage during the past five or six years. The institution houses infants up to 3½ years, between 150 and 200 at all times. I have found that the use of this vaccine has resulted in a decrease in complications, but the incidence of nasal discharge has not been influenced. The same number of so-called colds occurred in the inoculated and the control group. I believe our hope rests in the use of the virus, but a more important thing is that the "common cold" be more clearly defined. Must one not consider meteorological changes as well as a virus carrier in the Spitzbergen episode?

DR. YALE KNEELAND JR., New York: The defense of the common cold as an entity is a difficult one. It is perfectly true that the symptoms of allergic rhinitis are often indistinguishable from those of a flareup of chronic sinusitis or the common cold. Furthermore, there is no question but that there are numerous extraneous factors having nothing to do with infection, which can play a role, such as alterations in the physical environment. Looking at the problem in a very broad, general way, one is inevitably brought back to the experience of the observers who have made really careful studies of small, isolated communities. I think the clearest of those studies was the one made by Paul and Freese in Spitzbergen, where, in a population of about 500 persons exposed to the severities of the subarctic winter there were no colds during a period of seven months when the harbor was icebound and the community physically isolated from the outside world. When I say there were no colds, that is not strictly true. There were four, three occurring in the same person, who was thought to have a chronically infected sinus, and one occurring spontaneously in another person. There was no evidence that these four clinical episodes were communicable diseases. However, within seven days after the arrival of the first boat in the spring there were 125 examples of acute upper respiratory infection among the population. Bacteriologic studies made throughout the entire winter, during the spring when the first boat came, and during the outbreak showed no significant alteration in the flora, and the observers were unable to identify any new organism as having been introduced. The inevitable conclusion is that while these other factors undoubtedly have a role of considerable importance there is one essential factor—the virus—without which the whole structure doesn't exist in the form in which we know it. That is as far as we can go in defining colds. As to carriers, our own attempt consisted of one experiment in which we studied a number of normal persons in the summer. We found none of them to be carriers of virus. We have made no other studies ourselves. It would be of enormous importance to determine that point. As to a sudden weather change being responsible for the Spitzbergen outbreak, that is a possible point of argument. There is no way of proving that changes in atmosphere, barometric pressure and the like, associated with the ice going out, were not influential. However, my feeling is that meteorological changes exert a significant influence only in a system where the virus is present.

ENDEMIC TYPHUS FEVER IN NATIVE RODENTS

GEORGE D. BRIGHAM, PH.D.
AND
R. E. DYER, M.D.
Senior Medical Technician and Senior Surgeon, Respectively, United States Public Health Service
WASHINGTON, D. C.

Endemic typhus fever was first recognized in the Southern states in Atlanta, Ga., in 1913 by Paullin.[1] It was reported from Charlotte, N. C., in 1914 by Newell and Allan,[2] from Galveston, Texas, in 1916 by McNeil[3] and from southern Alabama in 1923 by Maxcy and Havens.[4] In the next few years, largely through the work of Maxcy,[5] it became evident that this form of typhus fever was widespread in the states of the South, from the Atlantic seaboard to the lower Rio Grande Valley. In discussing the geographic distribution of the disease in 1929, Maxcy[6] recognized the presence of endemic typhus in nearly all the seaports of this area and noted in particular that, while an "occasional case has been reported from the interior of the country, that section has been for the most part strikingly free." This author[7] also noted that the majority of cases occurred in the cities and towns, with practically no cases occurring in strictly rural districts.

From the National Institute of Health.
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The urban character of endemic typhus was also stressed by Rumreich [8] in his differentiation of cases of Rocky Mountain spotted fever from cases of typhus in the Eastern states in 1931.

From the time of recognition of the fact that typhus is not unusual in the South until 1932, there was a gradual increase in the number of cases recognized each year. Thus, in 1922 fifty cases were reported, and each succeeding year showed a small increase until 250 cases were reported in 1929, 500 in 1930 and 300 in 1931. This ten year period (1922 to 1931) showed the increase in cases that one might expect from an increased recognition of the disease by physicians. In 1932 the number of cases increased sharply to 831; the figures for the next three years were 1,922, 1,308 and 1,195, respectively. With the increase in the number of cases, the disease apparently lost something of its essentially urban characteristics. This was remarked on by Baker, McAlpine and Gill,[9] who noted in 1935 that much of the typhus in Alabama was in purely rural areas. These writers also reported that the rural cases were among people who could have obtained their infection only at home. This is in contrast to the increased prevalence of the disease among workers in food-handling establishments noted by Maxcy.[7] Furthermore, Rumreich,[10] in speaking of the increasing prevalence of cases in rural and semirural areas, voiced the suspicion that the disease might have become established in animals other than the common rat. He noted occasional cases occurring under conditions which did not suggest rats as a causative factor and indicated the probability that some other animal might be acting as a reservoir of the virus. These observations led him to inaugurate studies, in cooperation with the Alabama State Board of Health and the Rockefeller Foundation, to determine the susceptibility to typhus of animals that were native in the typhus-infected sections. These studies were begun in Montgomery, Ala., but were later moved to the field laboratory of the United States Public Health Service at Mobile, Ala., where they are now being carried on.

Beginning with Nicolle's [11] successful infection of monkeys in 1909, many animals have been found by various workers to be susceptible to infection with typhus, either of the epidemic, or louse-borne, type or of the endemic, or flea-borne, type. Nicolle transmitted typhus to the chimpanzee and to Macacus sinicus. Later, Anderson and Goldberger [12] reported that they were able to infect Macacus rhesus. In 1911 Nicolle [13] reported the infection of the guinea pig and in 1915 of the rabbit.[14] Some ten years later the gray rat [15] and the white rat, the white mouse and the gerbil [16] were added to the list by the same author. Spermophiles (Citellus citellus) were found susceptible by Lépine,[17] a finding that was confirmed by Combiesco [18] and by Jelin and Grossman.[19] Squirrels (Xerus [atlantoxerus] getulus) were successfully infected by Blanc and his collaborators,[20] while dogs were shown by Combiesco and Angelesco [21] to have inapparent infections when inoculated with typhus virus, and Lépine [22] found that cats were susceptible, often showing no sign of the infection. Bruynoghe and Jadin [23] tested the susceptibility of certain rodents to typhus. They found meadow mice (campagnols, Arvicola arvalis) and dwarf mice (souris naines, Mus minutus) susceptible, but failed to infect wood mice (mulots, Mus sylvaticus) and garden mice (lerots, Myoxus nitela). Ronse,[24] however, succeeded in infecting garden mice and wood mice and also hedgehogs (herissons) and pigeons. Ronse did not give any specific names.

In America, Dyer [25] found the woodchuck (Marmota monax monax), the house mouse (Mus musculus musculus) and two species of wild mice, the meadow mouse (Microtus pennsylvanicus pennsylvanicus) and the white-footed mouse (Peromyscus leukopus noveboracensis), susceptible.[26] The susceptibility of the woodchuck is apparently of academic interest only, so far as a possible relationship to the endemic typhus now present in this country is concerned, since this rodent does not inhabit the sections where typhus is prevalent. Of the groups of mice to which the two species of wild mice used by Dyer belonged, the leukopus group of white-footed mice is absent from the area of greatest incidence of typhus fever, while the meadow mouse is represented by several subspecies.[27]

In the investigations carried out in Alabama by one of us (Brigham) animals, chiefly rodents, were trapped in southern Alabama, principally in the southeastern counties—Houston, Dale, Henry and Geneva. These rodents were then taken to the typhus research laboratory in Mobile and tested for susceptibility to typhus. In this work the strain of endemic typhus known as the Wilmington strain was used. This strain was originally recovered by Maxcy [28] from a human being with the disease in Wilmington, N. C., in 1928. Testicular washings from guinea pigs infected with the Wilmington strain were used as a source of virus to infect the native animals. The testicles were removed from infected guinea pigs on one of the first three days of fever, usually the second or third, and washed with about 20 cc. of 0.85 per cent sodium chloride. The animals to be tested were then inoculated intraperitoneally with a variable amount of the washings, usually from 0.25 to 0.5 cc. for the smaller rodents. The larger rats were given 1 cc. and such animals as the opossum, cat and raccoon from 6 to 7 cc. Fresh guinea pigs were inoculated with some of the same material at the same time to prove its activity. At varying periods after the infecting inoculation, usually about ten to eighteen days, the test animal was killed and the brain removed. The

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brain was then ground up in a sterile mortar and, after suspension in a few cubic centimeters of saline solution, was injected into male guinea pigs. Two guinea pigs were regularly used for this test, each guinea pig receiving one half of the suspended brain when small rodents were under test. When larger animals were being tested, about 4 cc. of a heavy brain suspension was injected. The inoculated guinea pigs were observed daily for rise in temperature and scrotal lesions indicative of infection with typhus. When either of these indications developed, the guinea pigs were killed and their organs used to perpetuate the virus in other animals. The identity of all strains of virus recovered from inoculated native animals was judged by the usual criteria—clinical picture in guinea pigs, presence of Rickettsiae in smears from the tunica, production of agglutinins for Bacillus proteus OX_{19} in rabbits, development of typical histologic changes in the brain and a definite and complete cross immunity with the stock strain.

When the foregoing criteria were used, the following animals [29] were found to be susceptible: opossum (Didelphis virginiana),[30] old-field mouse (Peromyscus polionotus polionotus), cotton mouse (Peromyscus gossypinus gossypinus), golden mouse (Peromyscus nuttalli aureolus), wood rat (Neotoma floridana rubida), cotton rat (Sigmodon hispidus hispidus), rice rat (Oryzomys palustris palustris) and flying squirrel (Glaucomys volans saturatus). The virus was also successfully passed through a young cat, confirming Lépine's observations. Several attempts to infect raccoons failed.[31] The opossum used in this experiment was not identified as to subspecies, but since the animal was trapped about fifteen miles north of Mobile it was most likely a Florida opossum (Didelphis virginiana pigra). This subspecies occurs in Florida and along the Gulf Coast to western Louisiana.

The geographic distribution of the groups used in these experiments may be said to cover in general the area of greatest incidence of typhus in the United States. However, the susceptibility of these animals to laboratory infection and their presence in the area where endemic typhus occurs only indicates the possibility of their actually serving as a reservoir of the disease in nature.

During the period when the studies on the susceptibility of native rodents have been carried out at the laboratory in Mobile, repeated attempts have been made to recover the virus of endemic typhus from animals found in the area where typhus was showing its greatest rural incidence. For this work, as opportunities offered, traps were set on the farms where typhus had recently occurred or was present at the time. It was found that if a reasonable price was offered a number of animals greater than could be handled in the laboratory could be procured without difficulty. These animals, mostly small rodents, were brought in from time to time and kept in glass battery jars until they were killed in the attempts to recover typhus virus.

In this search for typhus virus, the brains of the wild rodents were removed and, after being ground in a mortar and suspended in salt solution, were injected into guinea pigs by the peritoneal route. To reduce the chances of introducing extraneous infections, the brains of rodents were not pooled, but each brain was kept separate and approximately half was injected into each of two guinea pigs. Therefore, few guinea pigs were lost as a result of other infections, and it is felt that the presence of the virus in any of the examined rodents was not overlooked. Daily temperatures were taken of all guinea pigs so inoculated for at least eighteen days after inoculation, and those that showed no signs of typhus infection after inoculation were later tested for immunity to the stock Wilmington strain of endemic typhus. No guinea pig so tested showed evidence of immunity.

On Sept. 7, 1936, an old-field mouse (Peromyscus polionotus polionotus) [32] was trapped on a farm in the western part of Houston County, in southeastern Alabama. The mouse was received at the laboratory two days later and placed in a battery jar with five other old-field mice which had been trapped at the same location. As the supply of guinea pigs and the press of other work permitted, these mice were removed from the jar and killed one by one. Thus, two mice, 86 and 87, were killed on October 16, two, mice 91 and 92, on October 29, and two, mice 93 and 94, on November 5, and their brains inoculated separately into guinea pigs. The guinea pigs which received the brains from mice 86, 87, 92 and 94 and one of the guinea pigs receiving brain material from mouse 91 showed no subsequent signs of infection and when later inoculated with the stock strain of typhus had typical attacks of typhus. The second guinea pig, inoculated with the brain material from mouse 91, had a febrile reaction on the fifteenth day after inoculation. On the fifth day of this reaction the guinea pig was killed and some of its blood and all of its brain used to inoculate four fresh guinea pigs. These four guinea pigs failed to show any signs of typhus and were later found to be nonimmune.

Both of the guinea pigs which were inoculated with the brain from mouse 93 had febrile reactions on the sixth day subsequent to inoculation and scrotal swelling, typical of endemic typhus, two days later. By transfer of blood and testicular washings from one of these guinea pigs, the strain was perpetuated and has been maintained in laboratory animals to date. Up to the present time this strain has been passed through 102 guinea pigs in twenty-five transfer generations. Of these animals eighty-seven have given a typical clinical picture of uncomplicated endemic typhus, eight have shown fever and only transitory scrotal involvement, two have shown fever only and five have died of intercurrent infections.

Comparison of the strain isolated from the field mouse with the Wilmington strain of endemic typhus showed no differences. In guinea pigs, the clinical reactions produced, the presence of Rickettsia in smears from the tunica vaginalis and the character of microscopic changes in the brain [33] were in all respects similar to what has been recorded for other typical strains of endemic typhus. In addition, agglutinins were produced for B. proteus OX_{19} in rabbits after inoculation with the field mouse strain, and complete cross immunity was observed between this strain and the Wilmington strain.

The field mouse from which the typhus virus was recovered was trapped in the western part of Houston County, Ala., this county being in the southeastern corner of the state. The mouse was trapped in a field that had not been under cultivation for several years,

29. Identification through the courtesy of the Division of Mammals of the National Museum.
30. Brigham, G. D.: Pub. Health Rep. **51**: 333 (March 27) 1936.
31. Brigham, G. D.: Pub. Health Rep. **52**: 660 (May 21) 1937.
32. Brigham, G. D.: Pub. Health Rep. **52**: 659 (May 21) 1937.
33. All histologic examinations of brains were made by Dr. R. D. Lillie, National Institute of Health.

at a location about one quarter of a mile from the nearest house. Thirteen other houses occupied by white tenants were within a radius of 1 mile of the location where the mouse was caught. No cases of typhus had occurred among the residents of these houses for the past five years. Outside a radius of 1½ miles and within a radius of 6 miles, thirty cases have occurred within five years. Four of these occurred among the inhabitants of a small town of 300 people. The remaining twenty-six cases were strictly rural. This particular section of Houston County is close to the border of Houston and two other counties, Dale and Geneva. These three counties have reported a total of 639 cases in the past five years, at least one third of which are classed as rural cases. The typhus-infected mouse was the eighty-seventh wild rodent examined for infection since the inauguration of the work in our Mobile laboratory. The recovery of the virus of endemic typhus from a wild mouse from this area suggests a possible explanation for the occurrence of so many rural cases, but, with the presence of other susceptible species of animals in the same area, the possibility of other reservoirs must be admitted.

SUMMARY

The incidence of endemic typhus fever in the southeastern part of the United States has increased, and there is a tendency toward a spread of the disease from the original foci in towns to the rural districts.

Eight species of animals, chiefly rodents native in the typhus-infected sections of the United States, are susceptible to typhus fever.

The virus of endemic typhus fever was recovered from a native rodent trapped in a rural section of Alabama.

Twenty-Fifth and E streets.

ABSTRACT OF DISCUSSION

DR. JOHN J. PHAIR, Baltimore: The substantiation of Rumreich's premise that the typhus fever virus may become established in animals other than the common rat, by the finding of the virus in a field mouse, is interesting. It indicates at least that the spread has begun and, when this is coupled with the further observations on the susceptibility of other animals, it will apparently have a fertile field in which to work. The typhus fever found in the endemic areas of the Southern states does not present the serious aspects that are common in the Old World type found in the colder zones where the disease is louse borne. It has a relatively mild clinical course and low fatality. The epidemiology of the disease has also some significant differences. However, the disease with its implications to the public presents questions that the public health workers of those areas must be able to answer. The usual answer, to eliminate the rat population, does not suffice for Southern rural communities. Rat eradication is an exceedingly expensive and laborious undertaking even in an urban community and is practically impossible in a rural area. It must be a continuous and unrelenting warfare and the effort cannot be relaxed after one or more sporadic drives; furthermore, this sort of service is beyond the powers of health departments of most of the areas in question at the present moment. Further work of the type that Dyer and his associates are doing is needed. We need rat surveys that will give adequate data to show the relationship between the number of rats in a community, the number infected and the amount of typhus. Rat control, rather than rat eradication, probably will be the method that will be most efficient; in other words, it might not be necessary to secure complete eradication but rather work toward a rat population level that would not be great enough to cause transmission of the virus. Rat control is a service that might be possible with the resources of the average health department. Rodent eradication is impossible, as health agencies cannot poison the entire wild life of a rural area.

DR. J. N. BAKER, Montgomery, Ala.: This paper is one naturally of considerable interest to any health officer in the South. It is of particular interest to me, coming from the state where a great deal of this experimental work is going on. Dr. Phair referred to the futility of rat eradication programs. This is true. It must be a relentless warfare and it must be a persistent one or else interest lags in the long run. When this happens, the problem is soon likely to revert to the status quo ante and no permanent gains are made. He also spoke of the possibility of health agencies, either in the state or in municipalities, trying to design programs thinking in terms of permanence so far as rat control is concerned; that is, the application of modern rat-proofing methods. That is the sound method of approach, if lasting results are desired. Several years ago, when Alabama first undertook an eradication program seriously throughout the southeastern portion of our state, we were able to have killed an enormous number of rats throughout the infected area, and we could see reflected a rather pronounced decrease in the incidence and in the mortality rate of the area; however, because of financial stringencies the program slackened considerably, with a resulting increase in the incidence of cases in the succeeding year. We now have set up in our central organization a control program of rat eradication through rat proofing, coupled with rat extermination, under the direction of a physician who has been well trained by the Public Health Service in the technics of the rat proofing of buildings. We are attempting to get as much of the new construction as possible going on in this area properly and scientifically rat proofed. As a consequence, in Mobile, Montgomery and several other municipalities we have made real progress in educating the public to the importance of rat proofing new structures and remodeling and revamping old structures to make them rat proof. I would suggest that other state health officers think in terms of setting up some such program. A significant fact regarding the incidence of endemic typhus both in Alabama and in Georgia is the almost exact coincidence of the areas involved with the peanut growing sections of these states. The growing of the peanut in southeastern Alabama and through the central segment of Georgia, projected on the Atlantic seaboard, is an important agricultural pursuit, and it is in these areas that most of our typhus occurs. However, more recently we have found that typhus has shown some tendency to spread to some of the more northerly counties, as several cases have been reported from Birmingham, in Jefferson County, where rat eradication and control programs have been begun.

DR. J. C. GEIGER, San Francisco: In our port city the U. S. Public Health Service many years ago initiated the rat proofing of buildings because of bubonic plague. At that time there was developed what was called a model rat proofing ordinance for buildings. This is still in effect. Such a measure is expensive, but it is a necessity. That it has delimited the rat population in San Francisco cannot be doubted. The problem of rat control in large cities and its relation to human disease is not limited to one disease. Bubonic plague is still a vexatious problem in California. San Francisco has not had a positive plague rat since 1908, and our control measures against the rat have been continuous. These control measures have been conducted by the U. S. Public Health Service and partly paid for by the department of public health. There are other problems regarding rats that are equally important to cities. Workers in San Francisco have investigated the problem of trichinosis and the relationship of the rat. More recently, Weil's disease has likewise come under scrutiny. In the vicinity of one case of Weil's disease, reported in San Francisco, there were found approximately 33 per cent of rats infected with spirochetes. It cannot be doubted that, because of its association with plague, trichinosis and Weil's disease, the rat is becoming a greater menace to the public health of large cities and quite expensive to the department of health in establishing control measures. I have increased my rat-catching forces 100 per cent this year because of the presence of Weil's disease. Plague in connection with rats in California has not

been forgotten, but scientific interest has been transferred to ground squirrels and other rodents. San Francisco had an outbreak of trichinosis several years ago. Investigation of the disease was done intensively and because of this San Francisco is regarded as one of the ports in the United States in which trichinosis is quite prevalent. It behooves the departments of health of other cities to investigate this public health problem. The departments of health of cities should have a definite rat control program and a technical knowledge of the examination of rats for the series of diseases which they are assisting to transmit to human beings today. It would appear that plague is moving toward the eastern part of the United States and across the mountains, being now demonstrable in Utah. With cities like Chicago in its path, there are public health problems of the highest magnitude with regard to rats and plague and other diseases. Therefore, cities of the United States, both inland and coastal, must give to these problems every consideration.

DR. G. H. COOMBS, Augusta, Maine: Four years ago a competent clinician decided during the convalescence of a patient living in an isolated section of the country, eight miles from the nearest village, that it must have been a case of endemic typhus. He still sticks to his conclusions. The only specimen of blood from this patient was obtained some four weeks after convalescence was established, when it came to my attention, and it was negative. This patient attended Holy Roller meetings in a nearby village situated at the mouth of one of our tidewater rivers, where the coal barges came in for the northern portion of the state, the coal being unloaded there. These meetings were the rendezvous for the roustabouts on the coal barges. There is a possibility there. The ice goes out of this particular river late in March. About six weeks ago one of our field workers was investigating an outbreak of scarlet fever. He was asked by the attending physician to see another case with a consultant. Diagnosis was held up because of its peculiar history. A man, aged 30, a laborer in a large manufacturing establishment on the tidewater section of the river, which received its coal from the Southern states, had a mild elevation of temperature, headache, backache, and a diffuse, macular, darkish red rash. The patient's blood was sent to the National Institute of Health, and the report was agglutination of 1 to 10 for tularemia and 1 to 80 for Bacillus proteus X_{19}. A second specimen at the end of ten days was reported as positive in an agglutination of 1 to 40 for Bacillus proteus X_{19}. We are engaged in a situation of watchful waiting. We feel that if there is some work we can do early we wish to do it. I am in hopes from this discussion and what I may learn on this trip to have some constructive ideas as to what we may do to control this situation.

DR. JAMES A. HAYNE, Columbia, S. C.: We have had typhus fever in South Carolina for some time. About four years ago an interesting paper was written by Dr. Mood of Charleston concerning sixty cases that occurred at Roper Hospital in that city. Each year a number of cases are reported, and last year 150 cases were reported. I am sorry to think that there are other sources of infection besides the rat, because we have all sorts of rodents in South Carolina and, if we are going to have something besides the gray rat to look for, we have more to do than we think we have at the present time. It is probable that there is a great deal more typhus fever in South Carolina than is reported. We made Weil-Felix tests on every specimen of blood sent in for a Widal test, but the physicians often send the specimens in such manner that we are unable to make the tests. The education of physicians in South Carolina as to laboratory methods seems still to be in the dark ages. They seem to forget as soon as they get out of medical school that there are such things as laboratory terms. They ask for typhoid vaccine when they mean typhoid bacterin and they ask for smallpox serum when they mean smallpox vaccine.

DR. JOHN A. FERRELL, New York: The study reported by Drs. Brigham and Dyer has been of particular interest to the health authorities of the country. I had not previously been fully acquainted with the scope of the study or with the results. Just as this study is of deep interest to the Southeastern states, studies being made by the Public Health Service in conjunction with the Northwestern states relative to sylvatic plague and Rocky Mountain spotted fever are extremely important to that region. As cases of these diseases have occurred beyond the international boundary, the western provinces of Canada are giving consideration to studies intended to determine to what extent these diseases have spread to Canada and as to whether or not they constitute a real public health menace to which Canada and its provinces should direct control measures. The public health organizations everywhere are in need of information which such studies may furnish for guidance in administrative matters.

THE TREATMENT OF PRIMARY CARCINOMA OF THE MALE URETHRA

HENRY A. R. KREUTZMANN, M.D.
AND
BEN COLLOFF, M.D.
SAN FRANCISCO

Carcinoma originating in the male urethra has always been considered a relatively rare disease. The first authentic case was reported by Hutchinson [1] in 1861. Bierbaum [2] fifty-one years later was able to collect only forty-nine cases from the literature. Goldstein and Abeshouse [3] in the early part of this year stated that up to the present time 112 cases had been described.

We have made a thorough search of the literature on this subject and have found 143 reported cases. Many of these had not been mentioned by any authors since their original publication. We have abstracted and tabulated each case history.

The object of this paper is to enumerate the various types of treatment used and to emphasize those giving the best results. This paper also includes two new cases, making a total of 145 reported to date.

In reviewing the histories, it was evident that the site of origin of the growth could not be accurately determined in many instances, as the malignant process had spread beyond its original source at the time the patient was first seen. This was particularly so when the bulbous or the membranous portion of the urethra was involved.

For clinical purposes therefore we have listed the growths into two main groups, depending on their location. In the first group are those occurring in the anterior, or penile, portion of the urethra, and in the second are those found in the bulbomembranous, or posterior, portion. Anatomically, the bulbous portion is not a part of the posterior portion. We have included it because the symptoms and physical signs of tumors located there are the same as those of growths occurring in the prostatic and membranous portions. From a study of the end results it is apparent that this arbitrary division is a perfectly rational one.

ANTERIOR PORTION OF THE URETHRA.

In sixty of the 143 cases studied, the carcinoma occurred in the anterior portion of the urethra. Various methods of treatment were used, such as (1) partial or complete amputation of the penis, (2) total or partial

From the Department of Urology, Mount Zion Hospital.
Read before the Section on Urology at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1937.

1. Hutchinson: Tr. Path. Soc. London **13**: 167, 1861.
2. Bierbaum, J.: Inaug. Dissert., Leipzig, 1912.
3. Goldstein, A. E., and Abeshouse, B. S.: Ann. Surg. **105**: 213-227 (Feb.) 1937.

emasculation, (3) x-ray treatment of the inguinal glands, (4) application of radium to the growth, (5) resection of the urethra and the growth, (6) external urethrotomy and (7) inguinal adenectomy in conjunction with one of the aforementioned forms of treatment.

Amputation of the penis, either complete or partial, was the treatment most often used. It was performed on twenty-nine patients, resulting in twenty-six recoveries and only three deaths. Treatment with radium or x-rays without surgical intervention was used on three patients,[4] two of whom were cured.

When the growth is limited to the distal anterior portion of the urethra, that is, the part in the region of the glans penis, partial amputation can be safely employed. If, however, the malignant process is in the shaft of the penis, near the bulb, and particularly if the corpora cavernosa are involved, it is best to perform radical amputation.

Emasculation is a needless operation and should never be done, as the testicles are not invaded with metastasis. Urinary infiltration of the scrotum due to rupture of the urethra has been reported. This may have led some surgeons to perform total emasculation.

It is surprising to note that of the sixty patients in whom the anterior portion of the urethra was involved thirty-four, or 56 per cent, recovered; fifteen, or 25 per cent, died, and in eleven cases, or 18 per cent, there was no mention of the end result.

POSTERIOR PORTION OF THE URETHRA

Seventy-eight patients had carcinoma of the posterior portion of the urethra; the growth was found most often in the bulbous or the membranous part and occasionally in the prostatic part. A study of the case histories showed many varied forms of treatment. Some no doubt were merely palliative, as the disease was too far advanced to permit constructive surgical intervention.

The different forms of treatment described were (1) suprapubic cystostomy, (2) internal or external urethrotomy, or both, (3) incision and drainage of the perineum, (4) resection of the urethra and the growth, (5) fulguration and application of radium, (6) excision of the inguinal or the deep femoral glands, (7) total emasculation, (8) passage of sounds and (9) use of an indwelling catheter.

In this series of seventy-eight patients only eleven, or 14.3 per cent, recovered, while fifty-eight, or 74.2 per cent, died. In nine cases, or 11.5 per cent, there was no mention of the end result.

The operation which gave the greatest number of cures was resection of the urethra with the included growth. This was performed in five[5] of the eleven cases. In one of the five the inguinal glands were also removed, in a second the penis was amputated and in a third radium was applied postoperatively.

In contrast to the gratifying end results obtained in the treatment of growths involving the anterior portion of the urethra, carcinoma of the posterior portion presents a gloomy picture. This is no doubt due to the fact that there are no characteristic symptoms of this disease. The patients are treated for stricture and its complications, such as rupture of the urethra, periurethral abscess or urinary fistula. By the time the true condition is recognized the growth has become inoperable.

Early diagnosis is essential. In studying the histories, we found it interesting that when more than one case was reported by the same author the diagnosis was made sooner in the second or third, owing to the physician's previous experience.

One should consider the possibility of carcinoma of the urethra in men after 40 who, with no previous history of stricture have the symptoms characteristic of this condition. Progressive difficulty on urination was an outstanding symptom. Hematuria occurred infrequently and then usually after instrumentation.

In patients known to have stricture, the development of periurethral swelling or periurethral infiltration of urine, with or without the formation of a fistula, should make one suspicious of malignant change. If there has been no recent instrumentation and therefore no possibility of traumatic rupture of the urethra, urethroscopy should be performed without delay. If polypoid tissue is found, a piece should be removed for biopsy.

In reviewing the entire series of 143 cases, we were interested to note that inguinal glands had been removed in only twelve cases, seven of anterior and five of posterior urethral involvement. In each instance except one the patient recovered. Of the forty-five patients in the entire series who recovered, only eleven had an inguinal adenectomy. In several patients the glands were seen on clinical examination to be enlarged. Sections after removal showed inflammatory changes but no metastasis.

Despite the fact that only approximately 4 per cent of the patients who recovered had an inguinal adenectomy, surgical intervention should include removal of the inguinal glands in order to obviate the possibility of metastasis by way of the lymphatics. Huggins and Curtis[6] described the surgical procedure in detail, and repetition at this time is needless.

The following reports are on two patients whom we have treated in the past three years:

CASE 1.—*History.*—An Italian, aged 52, unmarried, who complained of a weak stream, had been under treatment at intervals since February 1933 for a severe stricture involving the anterior portion of the urethra. Dilations were carried out to No. 30 F., and the patient was discharged in December 1933 as well. He came in at intervals to make sure the strictures did not recur. In May 1936 a grating sensation was noted when a No. 28 F. sound was passed. At that time the patient had no complaints. It was suspected that urinary salts had become deposited in the scarred area, and urethroscopy was performed. A papillomatous area involving the ventral portion of the urethra anterior to the bulb was observed. There was no bleeding, and the growth was circumscribed. A fragment of the growth, which broke off, was recovered and examined microscopically. The diagnosis of epidermoid carcinoma was made. Following endoscopy, a periurethral abscess developed involving the perineoscrotal region. The patient was admitted to the hospital on May 15.

Physical Examination.—The result was essentially negative. The inguinal glands were not enlarged or tender. The scrotum was reddened, enlarged and indurated, with no tenderness except at the raphe. The testicles and the epididymis were not distinguishable. Transillumination gave negative results. The penis appeared normal. The tone of the sphincter was poor, and a mass was palpable just inside of the sphincter. The prostate was not palpable, and there was no tenderness on rectal examination.

4. Wurmser, R.: J. d'urol. **24:** 497-521, 1927. Watson, E. M.: J. Urol. **21:** 217 (Feb.) 1929. Diehl, K.: Virchows Arch. f. path. Anat. **256:** 666-873, 1925.

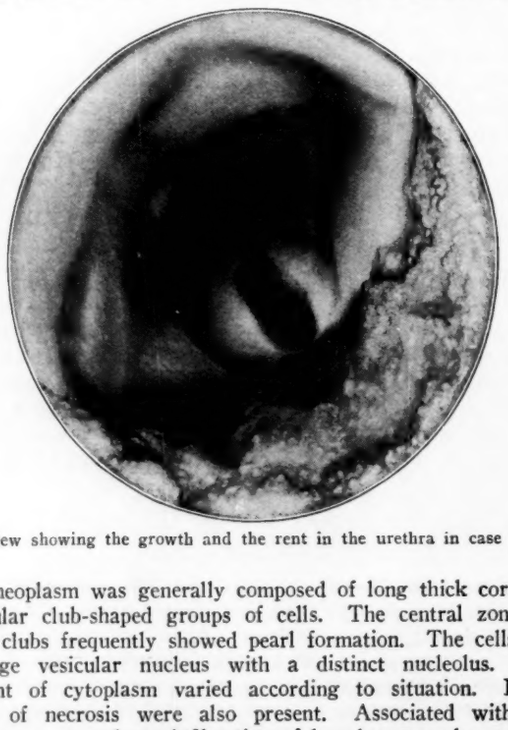
5. Lower, W. E.: Tr. A. Am. Genito-Urin. Surgeons **24:** 249, 1931. Sokolov, M. S.: Sovet klin. **18:** 265-272, 1932. Scholl, A. J., Jr., and Brasch, W. F.: Ann. Surg. **76:** 246 (Aug.) 1922. Oberländer, F. M.: Internat. Centralbl. f. d. Physiol. u. Path. d. Harn. u. Sexualorg. **4:** 244, 1893.

6. Huggins, C. B., and Curtis, G. M.: Surg., Gynec. & Obst. **44:** 544 (April) 1929.

Treatment.—With the patient under subarachnoid anesthesia a cystostomy was performed. A mushroom catheter was inserted and left in place. The scrotal abscess was then incised, and about 500 cc. of foul-smelling pus flowed out under pressure. Digital examination with a sound in the urethra revealed the presence of a mass on the left side of the urethra and an erosion of the urethra on the right. A drain was inserted. Resection of the urethra and a first stage ureteral transplant on the right side were performed June 18. The pendulous portion of the urethra containing the growth was removed.

This necessitated resection of the bulbous portion anteriorly for about 2.5 cm. The patient had refused amputation of the penis. A first stage ureteral transplant after the method of Winsbury and White was then performed on the right side. It had been our intention to anastomose the ureters, but the left one could not be found at this time.

Pathologic Examination.—Microscopic examination of sections of the penis showed the urethra to be irregular in outline and the normal epithelium to be replaced by stratified squamous epithelium in some regions. In other regions the epithelium was replaced by an ulcerated, irregularly proliferating squamous cell epithelioma. The regions lined by the stratified squamous epithelium showed that it had prominent rete pegs, and at the edges there was a transition into the neoplastic growth.



View showing the growth and the rent in the urethra in case 1.

The neoplasm was generally composed of long thick cords or irregular club-shaped groups of cells. The central zones of these clubs frequently showed pearl formation. The cells had a large vesicular nucleus with a distinct nucleolus. The amount of cytoplasm varied according to situation. Large areas of necrosis were also present. Associated with the neoplasm was a dense infiltration of lymphocytes, plasma cells and phagocytic mononuclear elements. The neoplasm seemed to be limited to the corpus spongiosum. In the fibrous tissue separating the corpus spongiosum from the corpora cavernosa there were perivascular infiltrations of lymphocytes and plasma cells, which were also seen in the corpora cavernosa. A section in another region showed no evidence of neoplastic invasion and did not include the urethra.

A diagnosis was made of squamous cell epithelioma of the urethra, with invasion of the corpus spongiosum, and metaplasia of the urethral epithelium.

Further Treatment.—August 5, with the patient under subarachnoid anesthesia, the ureteral transplants were completed. The second stage of the Winsbury-White procedure on the right side was accomplished without difficulty. A No. 8 ureteral catheter had been passed up the left ureter by means of a cystoscope passed through the suprapubic wound before the operation was begun. This greatly facilitated finding the left ureter, which was then transplanted by the method described by Hinman. Peritonitis developed, and the patient died five days later.

Autopsy.—The usual midline incision was made through a very thin layer of fat and firm muscle, which in the lower part of the abdomen followed the line of surgical incision. The omentum covered the intestine and was fixed on to the right side of the pelvis. Other adhesions to the incision and to the bladder also were seen. The peritoneal cavity contained purulent fluid both free and in several sacs. The stomach, the duodenum and the upper part of the jejunum were markedly dilated and partly covered with fibrinous exudate. The loops of the jejunum were adherent to one another in several places, and in the upper third of the ileum the adhesions were so dense that the resulting block had caused the dilatation of the intestinal tract above this point. A fibrinous exudate and injection of the vessels of the serosa were seen throughout the colon and the sigmoid flexure. The appendix was normally situated. No alteration could be noted in the appendix. The pelvic organs were normally placed.

Genito-Urinary Tract: The kidneys, ureters, bladder, prostate, testicles, urethra, sigmoid flexure and rectum were removed *en masse*. Both ureters were surgically implanted in the lower part of the sigmoid flexure. The left ureter had its orifice in the sigmoid flexure. In the right ureter there was an orifice into it. Near the insertion of the right ureter there was a small hole in the sigmoid flexure, and around this region a marked peritonic process was seen. Both kidneys were enlarged. The capsules were easily stripped. On section the pelvis of the right kidney, especially, was seen to be markedly dilated. Both pelves were filled with a purulent fluid. The mucosa of the pelvis contained many injected vessels. The parenchyma of the kidneys appeared normal. No regional glands could be found.

Microscopic examination of the right lung showed nests of epithelial cells in large regions of fibrosis. These cells were of flat epithelial type; they contained a dark nucleus with pale cytoplasm. Numerous mitotic figures occurred. No pearl formation was noted. Invasion of the epithelial nests above the region of fibrosis was noted.

The diagnosis was (1) cornifying squamous cell carcinoma of the urethra, (2) metastasis to the right lung, (3) generalized peritonitis and (4) bilateral pyelitis.

CASE 2.—*History.*—A white man, aged 44, a physician, who complained of weakness of the urinary stream and pain and swelling at the base of the penis, for the past sixteen years had had difficulty on urination. He realized that his illness was due to a urethral stricture resulting from an attack of gonorrhea contracted when he was 19 years old. This stricture had bothered him a great deal, but, being of a nervous, apprehensive nature, he did not consult a physician.

During January 1934 he sought treatment because of a littritis involving one of the glands near the base of the penis. This gland became suddenly swollen and was very tender. Poultices of magnesium sulfate were applied, and after twelve days the swelling subsided and the pain disappeared. Attempts were then made to dilate the urethra. Between January and April 1934, filiforms and tunnel sounds Nos. 8, 10 and 12 F. were passed. Because of the severe strictures along the urethra and the nervous condition of the patient, it was impossible to increase the size of the sounds beyond 12 F. In the latter part of April a second abscess developed at the base of the penis. Poultices this time were of no avail, and the patient was taken to the hospital, where, while he was under gas and oxygen anesthesia, the abscess was opened. It healed in approximately three weeks without any leakage of urine through the external wound. During May 1934 the patient had great difficulty in voiding, the stream was weak and dribbling and the condition at times verged on complete retention. Therefore the patient was taken to the hospital in the early part of June and prepared for an operation to relieve the urethral stricture. During his illness he had frequency, voiding every two or three hours and three or four times at night, with dysuria after instrumentation. He had never noticed any blood in the urine.

Physical Examination.—The inguinal glands were not enlarged at the first examination. Along the ventral surface of the penis four or five indurated nodules were palpable. There was a small scar at the base of the penis, which was

entirely healed. On palpation of the urethra in the perineum it appeared thickened, indurated and slightly nodular. The prostate was soft, and no areas of induration in the rectum were palpable.

Operation.—Anesthesia was induced by gas and oxygen. With the patient in the lithotomy position, an incision about 4 cm. long was made in the perineum. The superficial transversus perinei muscles were exposed and retracted posteriorly, exposing the bulb. An incision was made through the bulb down to the urethra. The urethra was seen to be thickened, and nodules could be plainly felt on the ventral surface. An incision 1 cm. long was made through the ventral surface, and the edges were caught and retracted. A mass of scar tissue was found immediately within the urethra. After some difficulty a filiform was passed from the external urethrotomy wound into the bladder. On to this filiform a urethrotome was threaded. This urethrotome, instead of having a knife blade, had a fine wire which coagulated at the same time as it cut. With the current turned on, the electrical urethrotome was passed into the bladder. After the cuts were made there was very little bleeding and it was possible to pass a No. 26 sound through the wound into the bladder. After this was done a filiform was passed from the meatus down through and out of the perineal wound. The urethrotome was then threaded on this filiform, four distinct cuts were made and a No. 24 sound was passed through the strictured area in the penile portion of the urethra. It had been planned to resect whatever scar tissue was necessary, but after the strictured areas were cut with the urethrotome it was unnecessary to do any resection of the urethra. A No. 22 Robinson catheter on a stylet was passed through the meatus beyond the external urethrotomy opening and into the bladder. The urethra was then closed with No. 1 chromic interrupted sutures, and the bulb was closed in the same manner. A small rubber drain was placed opposite the bulb, and the skin was closed with dermal sutures. A suprapubic cystostomy was then performed and a No. 24 mushroom catheter left in the bladder.

Course.—Because of the pain produced by the indwelling catheter and the nervousness of the patient, the catheter had to be removed within twenty-four hours after the operation. The patient was most difficult to control. He complained greatly of pain. His nervousness was controlled with bromides. About two and a half weeks after the operation a psychosis due to the bromides developed. When the medication was discontinued the patient's mind became normal. He complained bitterly of the suprapubic drainage, but this had to be left in because the perineal wound was very slow in healing. All instrumentations of the urethra, such as the passing of sounds, had to be done after the patient was given gas and oxygen. A month after the operation it was felt that the perineal wound was sufficiently healed and the urethra normal enough to permit the patient to void. The suprapubic tube was removed, a No. 16 soft rubber catheter was inserted through the urethra into the bladder and Connell suction was applied. Again the patient could not stand the pain of a urethral catheter, and it had to be removed the second day after insertion. The urine then drained through the suprapubic wound, and very small amounts were voided.

In the early part of August it was noticed that the glands in both inguinal regions were enlarged and indurated and that the skin over them was reddened. Compresses were applied. After several days of compresses, fluctuation was noted in the enlarged inguinal nodes on the left side, and, with 1 per cent procaine hydrochloride anesthesia, the abscess was opened and about 8 cc. of pus removed.

About this time also the perineal wound broke down, and the urine, instead of passing through the urethra, leaked out through the perineum. On Aug. 15, 1934, the patient was again operated on, after having been given 500 cc. of whole blood. While he was under gas and oxygen anesthesia, the perineal wound was opened. Greatly to our surprise we found that along the infected margins of the urethra rounded tissue had formed which at first looked like granulation tissue except that it was paler and did not bleed easily. Examination showed that this granular tissue had formed a line of cleavage between the layers of skin and muscle in the left inguinal region, so that the examining finger could feel this nobby, irregular growth as far as the inguinal glands on the left side.

It was recognized immediately that the condition was not a simple one but some type of malignant process. The urethra was followed down by elevating the transversus perinei muscles, and the whole area between the urethra and the rectum was found to be involved by the granular tissue. The recto-urethralis muscle could not be identified because the whole space between the urethra and the rectum was filled. The material was dissected as far as the prostate. The rectum was depressed and the urethra was retracted upward. This peculiar tissue could be felt as far as the prostate and extended on both sides. Because of the attachment and the position, it was impossible to remove all of it.

A fenestrated rubber tube was inserted down through the inguinal region and out through the perineal wound. A No. 26 soft rubber catheter was inserted through the suprapubic fistula into the bladder and held in place by a silkworm gut suture. The wounds were left wide open, and a piece of the new growth was removed for microscopic examination.

Pathologic Examination.—Sections showed a new growth composed of large masses of invading epithelium. In some regions the stroma was extremely scanty. In other regions the growth extended in fine strands into the fatty tissue, individual cords being separated by a varied though usually scanty amount of fibrous tissue. The cells of the growth were of medium size, with relatively large, clear-staining nuclei and a large amount of cytoplasm in the regions showing hyaline alteration. The cytoplasm was relatively scanty in the actively invaded portion. Cells in mitotic division were not infrequent.

The diagnosis was squamous cell carcinoma.

Further Course.—The patient was given eleven high voltage roentgen treatments over the bladder, perineum and inguinal regions. Although he was not told he had a malignant growth, the fact that he had these treatments made him very suspicious, and, being of a nervous neurotic type, he did not cooperate. Roentgenograms of the lungs at the time the roentgen treatments were given showed no metastasis. However, the patient became very morose, refused to eat, gradually became weaker and septic, and died on September 19.

SUMMARY AND CONCLUSIONS

Primary carcinoma of the male urethra is a rare disease, only 143 cases having been reported previously.

Reports of two new cases bring the total to 145.

For clinical purposes carcinoma of the male urethra is divided into two main groups, depending on the location of the growth.

The treatment of carcinoma involving the anterior portion of the urethra which has given the greatest number of cures is partial or complete amputation of the penis.

The best results obtained when the malignant process involved the posterior portion was resection of the urethra with the included growth.

Inguinal adenectomy is advisable in all cases.

Sufficient data have not been obtained up to the present time for one to evaluate roentgen and radium treatment without previous surgical intervention.

2000 Van Ness Avenue.

An Individual Kind of Superstructure.—You who are graduating here today, wherever you land—in laboratory, in hospital clinic, in practice—will have occasion to lament the insufficiencies of your preparation. This has been so from the beginning and will be so to the end of time. However secure the foundation may appear to have been laid, you will come to build on it an individual kind of superstructure which could not possibly have been anticipated.—Cushing, Harvey: Consecratio Medici and Other Papers, Boston, Little, Brown & Co., 1928.

THE MANAGEMENT OF TUMOR OF THE TESTICLE

FRANK HINMAN, M.D.
SAN FRANCISCO
AND
TRACY O. POWELL, M.D.
LOS ANGELES

Usually the general practitioner of medicine, not the specialist, first sees the patient with a neoplasm of the testicle. Although uncommon, such tumors are not extremely rare. Most of them are very malignant, and it is only by early diagnosis and proper treatment that any patients are cured. New methods of diagnosis and of treatment have made possible earlier recognition and better management, with the result that more patients can be cured than ever before. This recently accumulated knowledge has not become generally known. It is the present purpose to discuss briefly what would seem to be the logical management of the patient in the light of recent knowledge. Two illustrative cases of unusual interest are reported. An analysis of fifty-eight cases of tumor of the testicle, in all of which hormonal tests were made, forms the basis for the following outline of the seven steps of management. The majority of the fifty-eight patients have been observed for three years or longer.

1. *The Clinical History.*—The age of the patient, the character of the onset and the duration and course of the swelling are important points in diagnosis and prognosis. Men should be made as intelligent about tumors of the testis as women have been made about tumors of the breast. A patient who comes for advice as soon as the tumor is noticed has a better prognosis than the one who delays. In the past there has been entirely too much procrastination in seeking medical counsel; six months is the average period elapsing between the time the patient is first conscious of trouble and the time that he sees his doctor.

TABLE 1.—*Histologic-Hormonal Classification of Embryonal Tumors*

1. Teratoma	
a. Chorionepithelioma (primitive)	
b. Adenocarcinoma, etc.	
(1) Primitive	
(2) Differentiated	
c. Differentiated	
(1) With hormonal excretion	
(2) Without hormonal excretion	
2. Carcinoma	
a. Primitive	
(1) With lymphoid stroma	
(2) Without lymphoid stroma	
b. Differentiated	
(1) With hormonal excretion	
(2) Without hormonal excretion	

2. *The Physical Examination.*—There is a mass in the scrotum which gives the sensation of weight and does not transmit light. The other physical conditions may vary. These variable differentiating points will not be discussed, since they may be found in textbooks. It should be emphasized, however, that the practice by the physician of repeatedly palpating, examining and squeezing such masses is to be highly condemned. The danger of squeezing the cells of a malignant tumor into the lymphatics or blood stream is far greater at examination than at orchidectomy when that procedure is properly planned and carried out. Preliminary irradiation, with the idea of preventing metastases, is not only unnecessary but has many disadvantages.

3. *The Diagnostic Hormonal Test.*—The freshly voided morning urine is tested for gonadotropic hormone, and the finding of at least 300 mouse units per liter (M. U. L.) is strong evidence that the mass in the testicle is an embryonal tumor. If, however, the test shows less than this amount or is entirely negative, the possibility that the tumor may be malignant is not ruled out. About one fifth of the total number of our patients who subsequently were proved to have a malignant growth did not excrete the gonadotropic substance. When the hormonal test is positive, immediate orchidectomy is indicated for reasons given hereafter. When the test is negative but the clinical and physical evidence strongly points to tumor, orchidectomy is indicated as strongly. The older method of exploration and biopsy at the time of operation should be discarded.

4. *Early Orchidectomy.*—Orchidectomy should be radical, not exploratory, and the handling and squeezing of the scrotal mass should be avoided. The cord is exposed through a high inguinal incision as for herniotomy. It is then clamped and divided, all the lymphatic and vascular channels leading from the neoplasm being thereby severed. With traction on the cord the scrotal mass is freed by blunt dissection and delivered through the inguinal incision.

The advantages of early orchidectomy by this method are as follows:

(*a*) If metastases have not already occurred the operation will cure the patient, and even if they have it will prevent the further spread of malignant cells from the primary tumor.

(*b*) It furnishes the laboratory with the fresh tissue of the primary tumor unmodified by x-ray or other treatment. (1) Extraction of this material gives the most dependable information concerning the gonadotropic hormone and the most reliable check of the result of the previous tests of the urine. (2) Histologic study of the fresh tissue of the unaltered tumor (preferably fixed in Zenker's solution), in correlation with the results of the hormonal tests, permits a satisfactory classification of the neoplasm.

(*c*) With a classification based on a correlation of hormonal tests and the histologic study of the fresh tumor, one is better able to determine the prognosis and to outline the extent of further treatment, whether it is surgical, roentgenologic or both.

(*d*) The fact that irradiation of the scrotum has become unnecessary makes it possible for the roentgenologist to treat the patient with massive doses of x-ray with less danger of sterilizing him by accidental irradiation of the good testicle. This danger persists nevertheless, and the remaining testicle should be carefully screened during all roentgenologic treatments. Because of carelessness in this regard one of our patients, well otherwise, is sterile.

5. *The Correlation of Hormonal Tests with the Histologic Picture.*—A histologic study in over 100 cases of testicular tumor, in fifty-eight of which hormonal tests were made, shows that a correlation of these two studies helps greatly in the classification of tumors in relation to their radiocurability.

Histologically, in correlation with the hormonal tests, three main groups of tumors are recognized: (1) embryonal tumors with hormonal excretion, (2) adult tumors without hormonal excretion and (3) miscellaneous tumors, which are rare and cannot be classified

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into either of the other two groups. Only embryonal tumors cause the excretion in the urine of the gonadotropic hormone. The more embryonal and primitive the tumors are the more active will they be in the formation of the hormone. As they become differentiated and adult in type, less and less of the hormone is formed until so little may be excreted as to fail of detection by animal test. In this connection it should be noted that the amount of hormone which is formed is proportional to the total mass of the tumor which is present. A small amount of tumor tissue will form less hormone than a large tumor of the same type. The histologic and hormonal evidence, therefore, must be correlated in connection with the clinical picture. In this correlation a series of hormonal tests is useful. By a series is meant (*a*) the hormonal test of the urine before orchidectomy, (*b*) the hormonal test of an extract of the fresh tissue obtained by orchidectomy and (*c*) periodic hormonal tests of the urine after orchidectomy and during or following irradiation. The disappearance of the hormone from the urine after either operation or roentgenotherapy is not nearly so significant as its persistence. Persistence at a pathologic level (400 M. U. L. or higher) indicates unquestionably that residual neoplastic tissue is present, while the disappearance of the hormone does not always mean the absence of malignant cells.

The practice in certain clinics of giving massive doses of x-rays to the primary tumor in the testicle before surgical removal largely destroys the information which can be obtained by the foregoing series of tests. Some cures by irradiation have been reported without orchidectomy—but also without histologic confirmation of the diagnosis. Irradiation before operation is likely to make it impossible to get good histologic sections for microscopic study after orchidectomy. In the interpretation of hormonal tests it should be remembered that irradiation either by actual destruction of cells or by inhibition of their ability to secrete may cause a considerable reduction in the amount of hormone excreted.

Histologically, the embryonal tumors are subdivided into monocellular and mixed-cell tumors, the old subgroups recognized by Chevassu as seminoma and teratoma. Among the monocellular tumors, more universally called embryonal carcinomas, are varieties with a primitive type of cell and other varieties with a more adult and fully differentiated type; some of the latter do not cause the excretion of the gonadotropic hormone in the urine. The same condition is found among the embryonal mixed-cell tumors, or teratomas. The most primitive of these is the chorionepithelioma, which has the highest hormonal output of any tumor, whereas, the most fully differentiated tumor of this group, the fully differentiated teratoma, causes little or no excretion of hormone.

The histologic-hormonal classification of the embryonal tumors, fully differentiated forms of which are without hormonal excretion, is shown in table 1.

The value of the hormonal test in correlation with the histologic picture is twofold: first, in prognosis and, second, in treatment. Correlation gives greater ability in predicting the outcome and in determining more definitely the presence or absence of metastases, which together form the most reliable guide to subsequent surgical intervention or irradiation.

6. *Prognosis.*—As a whole, embryonal tumors of the teratoid group (table 2) are radioresistant and very malignant and afford a poor prognosis. The true adult teratoma (not embryonal) is clinically benign, although potentially malignant, and early surgical removal will effect a cure. The primitive types of the carcinomatous group of embryonal tumors (monocellular) are very malignant and, although highly radiosensitive as a rule, indicate a poor prognosis. Fortunately about 50 per cent of testicular tumors belong to the differentiated type of the carcinomatous group of embryonal tumors. This group affords the best prognosis. The hormonal excretion is low, and the patients, as a whole, respond well to irradiation (table 2).

7. *Subsequent Treatment.*—The six steps which have been given in the management of tumor of the testicle cover the treatment of this condition up to the point of subsequent treatment, since they have in mind throughout the cure of the patient. Early diagnosis and prompt orchidectomy offer the surest cure. The procedures to be followed afterward depend on the results. In the absence of demonstrable metastases and of the gonadotropic hormone previously present, further treatment at the time is not indicated. The patient is advised to return periodically (every three months) for physical examination and a hormonal test

TABLE 2.—*Analysis of Fifty-Eight Cases of Testicular Tumor in Which Hormonal Tests Were Performed*

Histologic Classification	Number of Cases	Hormonal Excretion, M.U.L.* (Average)	Response to Irradiation	Prognosis	Result	
					Dead	Alive
A. Embryonal tumors (hormone present)						
I. Teratoid (mixed-cell)						
a. Chorionepithelioma	2	20,000 to 3,000,000	Fair	Poor	2	0
b. Adenocarcinoma	6	2,000 to 1,000,000	Fair	Poor	6	0
c. Differentiated (with carcinomatous elements)	6	1,000 to 200,000	Fair	Poor	5	1†
II. Carcinoma (monocellular)						
a. Primitive	7	1,000 to 1,000,000	Good	Poor	5	2‡
(1) Without lymphoid stroma						
(2) With lymphoid stroma						
b. Differentiated	26	1,000 or less	Good	Good	4§	22
(1) With hormonal excretion						
(2) Without hormonal excretion						
B. Adult tumors (hormone absent)						
Adult teratoma	3	None	Poor	Good	0	3
Adult seminoma	8	None	Good	Fair	1#	7
C. Miscellaneous tumors	0	None				

* Mouse units per liter of urine.

† Patient living 5 years afterward; irradiation excellent; abdominal metastases have disappeared; hormone now 250 M.U.L.

‡ Patient 1 living two years afterward; irradiation fair; well; no metastases. Patient 2 living two years afterward; irradiation fair; well; no metastases; hormone 100 M.U.L.

§ Patient 1 lived three years; irradiation fair; died with extensive abdominal metastases; hormone always below 500 M.U.L. Patient 2 lived six years; irradiation excellent; died of widespread metastases; hormone always below 350 M.U.L. Patient 3 lived one and a half months; irradiation fair; died of metastases; hormone absent. Patient 4 lived three years; irradiation fair; died of metastases; hormone very low.

Patient lived three years; irradiation fair; died of extensive metastases; hormone always absent.

of the urine. With the appearance of metastases clinically or the recurrence of the hormone in the urine, treatment should follow the indications given by the histologic classification of the tumor correlated with the series of hormonal tests up to this time.

When metastases can be observed clinically, radical surgical treatment of any kind is useless and intensive irradiation alone is indicated. When metastases cannot be demonstrated clinically and the hormonal test remains positive or becomes so after orchidectomy, the most probable location of the metastases is in the primary and secondary lymph zones of the testicle. If the tumor is radiosensitive, as shown by its histologic-hormonal classification, this area should be intensively irradiated. If the probable response to irradiation of the metastases presumed to be in the primary lymph zone is estimated by the foregoing classification to be only fair or poor, then after irradiation an attempt radically to remove the lymphatic area should be made. Radical operation was performed on only three of the fifty-eight patients discussed in this report. All are living and well (no metastases clinically; hormonal tests negative), one seven years, one three years and one two years after the operation.

REPORT OF TWO UNUSUAL CASES OF CHORIONEPITHELIOMA

CASE 1.—A man, aged 38, received a severe blow from a door knob on his right testicle in August 1933. This caused excruciating pain. Considerable swelling followed the injury, and a hard mass developed in his scrotum and remained for several weeks. Within a month or so after the mass appeared, gynecomastia gradually developed, together with an increase in sexual libido and an increase of hair on his chest. The patient's physician examined him carefully, including his testes, and found no convincing evidence of testicular neoplasm at that time. In October the scrotal mass was removed surgically and found to be malignant. The patient was then referred to our clinic. Considering the fact that the tumor mass had been removed and no metastases could be discerned physically or from roentgenograms, the hormonal tests (10,000 M. U. L.) indicated a high hormonal level. After the use of roentgen therapy the hormonal level dropped, but the hormone never disappeared from the urine. Three months later the excretion of hormone became increasingly elevated, and a metastatic node was palpated in the left supraclavicular area. Again heavily filtered radiation at 850 kilovolts was used. The patient did not tolerate this treatment well, and it was discontinued before the course had been finished. Although he soon felt well again, his hormonal excretion rapidly increased. He died on Nov. 26, 1934. The urine recovered from the bladder at the autopsy, as well as the tissue juices, was found to contain 1,000,000 mouse units of gonadotropic hormone per liter. (We knew of no other instance of as high a urinary titer.)

Chief Points in the Necropsy.—The original tumor was of mixed-cell type, with high hormonal urinary output. Some of the areas appeared relatively benign. Sections from tissue removed from the lungs showed chorionic elements. Sections from metastases in the retroperitoneal lymphatics and the liver showed a primitive type of unicellular tumor. There were no metastases below the external iliac vessels. The prostate was not enlarged in spite of the high saturation with gonadotropic substance. The anterior pituitary body was strikingly eosinophilic.

CASE 2.—Another of our patients with tumor of the testis had gynecomastia and a high urinary titer (1,000,000 M. U. L.), but at the necropsy no definite chorionic elements were found. The other observations at necropsy were almost identical with those in case 1.

The absence of chorionic elements, with all other features so similar, would seem to indicate that primitive tumors, whether mixed or unicellular, are essentially the same biologically. This relationship is not found in the more adult and differentiated types of the two groups. The differentiated types of the unicellular tumors behave differently from the more differentiated mixed-cell tumors containing embryonal malignant elements (table 2). The fully differentiated monocellular tumor (seminoma) without hormonal excretion apparently affords a poorer prognosis than the most differentiated embryonal carcinoma, which is similar to it histologically but causes hormonal excretion; the adult mixed tumors without hormone are practically benign as compared with the more differentiated or adult-like teratomas with hormonal excretion. The latter indicate a poor prognosis.

SUMMARY

Fifty-eight cases of tumor of the testis were analyzed and the tumors grouped according to a histologic-hormonal classification. In two unusual cases of primitive tumor the urinary hormonal titer reached 1,000,000 mouse units per liter. The steps to be followed in the logical management of tumor of the testis are (1) clinical history, (2) physical examination, (3) hormonal test of the urine, (4) orchidectomy, (5) histologic-hormonal classification of the tumor, (6) prognosis and (7) subsequent treatment.

384 Post Street.

RENAL CARCINOMA

A STUDY OF NINETY-FIVE CASES, WITH FOLLOW-UP NOTES ON THIRTY-SIX

THEODORE R. FETTER, M.D.

PHILADELPHIA

This study embodies a clinical résumé of ninety-five cases of renal carcinoma (table 1). Thirty-one (32.63 per cent) of this number were studied at necropsy. In seventeen (17.89 per cent) of these the condition was discovered as a chance observation; ten patients (10.43 per cent) died after irradiation and four (6.31 per cent) postoperatively. Fifty-three (55.78 per cent) had a nephrectomy, four (4.21 per cent) a nephroureterectomy and one (1.05 per cent) a biopsy of a supposedly retroperitoneal mass which was in fact a renal neoplasm with extensive local metastasis. Seventeen (29.82 per cent) are living and with the exception of four (7.01 per cent) are in good health. Thirty-six (63.15 per cent) are dead; this number includes six (10.52 per cent) who died postoperatively. The remaining thirty (31.57 per cent) lived from less than one year to ten years and five months. Four (7.01 per cent) patients were not traceable. Eleven (11.57 per cent) refused treatment, had a carcinoma considered inoperable or left the hospital; no attempt was made to ascertain their present status. In many cases it was necessary to utilize the bureau of vital statistics of several states.

There were sixty-seven (70.52 per cent) males and twenty-eight (29.47 per cent) females (table 2). It is interesting to note that the four children (4.21 per cent) in the series were girls. The right kidney was affected in forty-eight cases (50.52 per cent) and the left in thirty-nine (41.05 per cent); in six (6.31 per cent) the affected kidney was not stated. In two cases

From the Department of Urology, Jefferson Medical College, and Jefferson Medical College Hospital.

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(2.1 per cent) there was bilateral involvement; the condition was noted at necropsy, a primary carcinoma in one kidney with metastasis to the opposite kidney. The ages ranged from 7 months to 84 years, the greatest number of cases occurring in the decades from 40 to 70.

PATHOLOGY

Needless to say there still exists much confusion as to the origin of renal carcinomas, and consequently there is a lack of agreement on their classification. In Jefferson Hospital, Dr. Baxter L. Crawford has interested himself for many years in the study and classification of malignant renal tumors in adults. Of this group of ninety-five tumors (table 3), ninety were classified as carcinomas and one as probably a hypernephroma. The four children had either a mixed tumor or an embryonal type of carcinoma.

Discussions have appeared in the literature as to the origin of malignant tumors of the kidney in adults since the theory was advanced by Grawitz in 1883 that the tumors arise from adrenal rests in the kidney. It is evident that many authors use the term "hypernephroma" to include all tumors of the kidney of a certain type, without reference to their origin. Crawford[1] suggested that there would be much less confusion if the term were used to refer only to the tumors which are considered to have originated from adrenal tissue. The consensus at the present time of persons who have made careful studies of large groups of these tumors is that the vast majority are true renal carcinomas and not adrenal tissue tumors. In histologic study of the majority, true columnar epithelial cells forming definite acini and papillae may be demonstrated. Crawford further pointed out the comparative infrequency with which adrenal rests are observed in the kidney and the frequency with which adenomas in various stages of development, which may become malignant, are found. In a series of over 3,000 autopsies at Jefferson Hospital one adrenal rest in the kidney and twenty-nine benign tumors of the kidney (adenomas) were observed.

TABLE 1.—*Outcome in Ninety-Five Cases of Renal Neoplasm*

	Number	Percentage
Necropsy	31	32.63
Chance observation	17	
Following irradiation	10	
Postoperative deaths	4	
Operation	58	61.05
Nephrectomy	53	
Nephro-ureterectomy	4	
Biopsy	1	
Living (operative series)	17	29.82
Dead (operative series)	36	63.15
Untraced (operative series)	4	7.01
Untreated	11	11.57

Waters[2] mentioned these tumors as "cortical renal tumors"; another term, "hypernephroid tumors," was suggested by Lubarsch.[3] Braasch[4] recently suggested that carcinoma of the cortex may be divided into two groups which have distinct clinical characteristics, namely, adenocarcinoma (hypernephroma) and alveolar carcinoma. There is no doubt that the general tendency today, particularly among genito-urinary surgeons, is to study the more practical considerations of diagnosis and management rather than to indulge in continued and ofttimes acrimonious discussion of the classification and terminology.

It is often noted, and correctly so, that the proper evaluation of histologic study of renal carcinoma does and should influence the prognosis. However, unless one has had a large experience in the study of renal tumors, this evaluation becomes increasingly difficult. Crawford stated that there are three main types of carcinoma of the kidney in addition to adrenal cell tumors: true adenocarcinoma, in which definite acini lined by columnar epithelial cells and resembling tubules may be found; the papillary type of carcinoma, composed of a somewhat flattened transitional type of epithelium which usually arises from the pelvis of the kidney or a calix, extending into the kidney structure, and the more or less solid type, composed of large undifferentiated clear cells arranged to form alveoli, with a small amount of fibrous tissue framework. The last type is the one which most closely resembles hypernephroma and is usually so classified, but the type of cell is entirely different from that found in adrenal tumors, and in many of these true tubule formation and columnar cells may be demonstrated.

TABLE 2.—*Age and Sex of Patients; Location of Neoplasm*

	Number	Percentage
Sex		
Males	67	70.52
Females (including 4 children)	28	29.47
Affected kidney		
Right kidney	48	84.21
Left kidney	39	68.42
Unknown	6	10.52
Bilateral (necropsy)	2	3.50
Age		
0-10 years	4	4.21
Age, years		
0-10	4	4.21
11-20	2	2.10
21-30	2	2.10
31-40	5	5.26
41-50	27	28.42
51-60	27	28.42
61-70	22	23.15
71-80	5	5.26
80 plus	1	1.05

SYMPTOMATOLOGY

The triad of symptoms hematuria, mass and pain was present in eighty-two (86.31 per cent), thirty-seven (38.94 per cent) and fifty-two (54.73 per cent) cases, respectively. A typical pyelographic filling defect was noted in forty-nine cases (51.57 per cent). Pyelography was not practiced on patients who were obviously very ill or toxic or in the late stages of the disease. Anemia, loss of weight and weakness were variable. When the latter triad is present and dominates the clinical picture, it is well to suspect a renal malignant growth. In my study it was interesting to note the relative frequency of the variability of the clinical features of each case in contrast to the usual textbook description. Toxemia was observed in many cases, due to variable causes, intercurrent illness, metastasis or uremia. Interestingly enough, several patients had no symptoms referable to the urinary tract other than the presence of a mass in the abdomen.

In several cases nausea, vomiting and gaseous distention were the only symptoms, and the patient was

1. Crawford, Baxter L.: Tumors of the Kidney, Pennsylvania M. J. **35**: 629-630 (June) 1932; The Classification of Tumors of the Kidney with Especial Reference to the Malignant Tumors in Adults, Am. J. Path. **8**: 615 (Sept.) 1932; personal communication to the author.
2. Waters, Charles A.: Preoperative Irradiation of Cortical Renal Tumors, Am. J. Roentgenol. **33**: 149 (Feb.) 1935.
3. Lubarsch, O.: Die destruirenden Nierengewachse, in Henke, F., and Lubarsch, O.: Handbuch der Speziellen Pathologischen Anatomie und Histologie, Berlin, Julius Springer, vol. 6, part 1, p. 630.
4. Braasch, William F., and Griffin, Miles: Prognosis in Renal Carcinoma, J. A. M. A. **106**: 1343-1346 (April 18) 1936.

in the hospital primarily for study of the gallbladder. One patient had a cough with hemoptysis, and later, when he was admitted to a tuberculosis sanatorium, a mass was found in the abdomen. He was operated on and an adenocarcinoma of the right kidney removed, from which there was metastasis to the lung. He died postoperatively. Chills followed by fever were noted in seven cases. Fever was variable in a great many of the other cases and was probably due to necrosis or hemorrhage in the renal carcinoma. In evaluating

TABLE 3.—*Pathology*

	Number	Percentage
Entire Series, 95 Cases		
Adenocarcinoma	76	80.00
Papillary carcinoma	5	5.26
Papillary adenocarcinoma	4	4.21
Cyst adenopapillary carcinoma	2	2.10
Squamous cell papillary carcinoma	3	3.15
Hypernephroma	1	1.05
Embryonal carcinoma	4	4.21
Operative Series, 57 Cases		
Adenocarcinoma	39	68.42
Papillary carcinoma	5	8.77
Papillary adenocarcinoma	4	7.01
Cyst adenopapillary carcinoma	2	3.50
Squamous cell papillary carcinoma	2	3.50
Hypernephroma	1	1.75
Embryonal carcinoma	4	7.01

symptoms it is important not to overlook other systems for the cause of variable symptoms. In a few cases other lesions were found in the genito-urinary tract, gallbladder and gastro-intestinal tract.

DURATION OF SYMPTOMS

The duration of symptoms before aid was sought is indeed variable. It is difficult to average the approximate time from the onset of the first symptom to the time of treatment. In one case hematuria was noted in August 1925, and a diagnosis of renal tumor was made. Nephrectomy was advised and refused. After a second attack of hematuria, in November 1927, nephrectomy was done. The diagnosis was adenocarcinoma of the kidney, with no metastasis, and radiation therapy was employed. Metastasis to the lumbar vertebrae developed in 1933, and the patient died in November 1936. Clinical investigation of this type is valuable because of the accuracy of the known facts. The average duration of time of symptoms apparently is from less than one year to three years; needless to say there are cases in which it goes beyond this period. In one case with which I am familiar, hematuria was present for seven years before operation; in another case, also known to me, a mass in the abdomen was present four years previous to nephrectomy. Optimism in the prognosis in the majority of cases of renal neoplasm is possible if one considers the element of time elapsing after the appearance of the first symptom, establishes the diagnosis early and institutes the proper therapeutic measures immediately.

One is impressed with the fact that there is still a great deal of procrastination on the part of the physician in recommending a thorough urologic investigation to the patient when hematuria occurs for the first time. It is evident that the sequence is not particularly different when one reviews the records from 1921 to 1930 and those from 1931 to 1937 in regard to the duration of time between the onset of hematuria and the diagnosis and treatment. I have attempted to average this time and find that it is anywhere between fourteen and twenty-eight months. In the presence of an abdominal mass and hematuria, the chances of the patient's receiving special attention early are proportionally greater. If toxemia, loss of weight and weakness, in conjunction with hematuria or a demonstrable abdominal mass, predominate, the physician may recommend immediate hospitalization. The urologist is then confronted with the end result and may have an opportunity to observe an interesting necropsy.

DIAGNOSIS

The diagnosis of renal neoplasm resolves itself into three distinct phases. A complete clinical history is absolutely essential, particularly if hematuria is a prominent symptom. One must emphasize the need for a complete physical examination. It may seem superfluous that it is still necessary to stress these fundamental requirements. It is not the purpose of this discussion to outline the method of procedure that should be followed to obtain this necessary information; every physician is or should be familiar with it. One is not surprised that the patient becomes a "neurotic" and looks for relief to agencies outside the realm of medicine, because the physician fails to carry out the most basic fundamentals of his training. The third phase of the diagnosis, a complete urologic examination, includes methods with which urologists are all familiar; namely, cystoscopy, retrograde pyelography, intravenous urography and renal function studies and urine, blood and dye elimination tests. Despite the fact that with the advent of pyelography it was assumed that there would be no more preoperative errors, one still sees occasionally that more minute attention on the part of the roentgenologist and the urologist must be given to this procedure.

Numerous authors report on the use of intravenous urography for diagnosis of renal tumors. I believe that one should be careful in placing too much faith in the interpretation of intravenous urograms in the case of renal tumor. One must recognize the fact that the better results in preoperative diagnosis due to the use of the excretory urogram occur in clinics where there is thorough appreciation of the shortcomings of urography.

TABLE 4.—*Signs and Symptoms*

	Number
Hematuria	82
Pain	53
Mass	43
Typical pyelographic defect	40
Chills and fever	14
Fever	Variable
Gastro-intestinal symptoms	5
Toxemia	Variable
Anemia	Variable
Weakness	Variable

When a precise and minute detail of the kidney pelvis and its calices is needed the retrograde pyelogram is still the best method of approaching a more correct diagnosis of renal tumor.

The method of procedure of retrograde pyelography in Jefferson Hospital has not varied since 1912, when the late Prof. Willis F. Manges first described the advantages of injection of opaque solution into the renal pelvis under fluoroscopic control. Dr. Manges,[5] in his paper on the subject, said "Pyeloscopy is a

5. Manges, Willis F.: Recent Advances in Pyelography, Am. J. Roentgenol. 5: 165 (April) 1918.

preliminary to pyelography and adds, we believe, distinctly to the comfort of the patient as well as to the safety and accuracy of the entire procedure." This statement is just as applicable today as it was when it was written. The highest degree of efficiency of a retrograde pyelography can be attained by practicing pyeloscopy.

A word as to the technic that may be followed in obtaining excellent retrograde pyelograms may be worth while. Careful preparation of the patient and a preliminary roentgenogram are important requirements. The roentgenogram should be of such quality as to show the outline of the kidney under investigation if it is anywhere near normal as to size, shape and position. Previous knowledge of variations in these respects helps one in injecting the opaque solution to produce the best possible pyelograms.

In all the cases in which a retrograde pyelogram was made, injections were done under fluoroscopic visualization. This method is of particular advantage in the diagnosis of tumor of the kidney and in the differentiation of renal and extrarenal masses, since one can see the effect of palpation. If a mass is palpable, one determines with certainty whether it is part of the kidney or independent of it. Palpation is done either before the pelvis and calices are completely filled or after the pyelographic films are exposed.

One must be certain that the opaque solution has free access to the pelvis and calices and then observe the action of the pelvis and calices during the filling process. If there is a suggestion of deformity, one should determine whether the solution will run by the catheter into the bladder; if it does there is little risk of overdistention of the pelvis with moderate pressure over the course of the ureter. The study may then be deliberate and several films be exposed. If there is no reflux the injection must be made very slowly and carefully, so as not to produce pain and spasm of the pelvis and calices. I have repeatedly seen rapidly emptying pelves, and on several occasions I have seen the calices empty while the pelves remained filled; in one instance one calix, the upper, filled and emptied repeatedly during the injection, independently of the other calices and the pelvis. Pyelograms are made rapidly by placing a casette on the abdomen of the patient and exposing through a small diaphragm opening, with the tube under the table. Such exposures are made in a fraction of a second and at any moment during the injection when conditions are favorable. My associates and I then make pyelograms of the entire urinary tract with the aid of the Potter-Bucky diaphragm.

The interpretation of pyelograms requires the combined skill of the roentgenologist and the urologist. As all urologists know, the diagnosis of renal tumor depends on some degree of deformity in the pelvis or the calices as revealed by the injected opaque solution. There are several types of deformities. First, and perhaps most characteristic, is the elongation of one or more calices, a condition which must be differentiated carefully from reduplication of the pelvis, especially when it involves the upper pole. The next most common deformity is the complete obliteration of one or more calices, with the defect having, as a rule, a smooth outline at the base of the calix or at the adjacent pelvis. Cystic tumors are apt to produce such a deformity. It may involve more than one portion of the pelvis and calix outline. Frequently there are small, crescent-shaped borders of the shadow of the opaque fluid. These are only diagnostic when they are constant in a series of exposures. Another type of deformity, the third, is dilatation of a calix due to pressure obstruction at a proximal point. One calix may dilate to a large extent and perhaps all the rest of the pelvis and the calices, so that all of the natural shape of the pelvis is distorted and the opaque solution seems to take on a wavy appearance throughout a considerable area.

The difficulty in interpretation comes mostly no doubt with the first type, elongation of perhaps only a single calix. In addition to the elongation the lumen is narrowed, and the narrowed lumen of a somewhat elongated calix has just the same appearance as a normal calix in a state of contraction. I depend entirely on serial exposures to determine whether the lumen is constant; and of course I also have the benefit of fluoroscopic observation during the injection. When more than one calix is involved, the problem is increasingly less difficult.

In the other three types of deformity the success of the interpretation depends entirely and only on the production of pyelograms that really demonstrate the size and the shape of the lumen of the pelvis and calices. One frequently cannot differentiate a cystic tumor and a solid one unless one can palpate the mass.

The differential diagnosis of extrarenal tumor is based entirely on palpation during the injection under fluoroscopic control. This is true also in the case of a rotated kidney; that is, the kidney may be rotated in such a manner as to give abnormal shape and arrangement to the shadow of the opaque solution. In such instances one can, by viewing the kidney fluoroscopically from a variety of angles, differentiate a normally rotated kidney from an abnormal one.

In investigation of the urinary tract one must constantly bear in mind that a lesion other than neoplasm may be present. Calculus, tuberculosis and cystic disease may be found in the upper part of the urinary tract; prostatism, neoplasm, diverticulum and calculus may be observed in the lower part. In the case of extrarenal lesions one must keep in mind the gallbladder, the gastro-intestinal tract and the retroperitoneal space. The differential diagnosis of retroperitoneal masses from renal neoplasms is difficult because of the possibility of extension of the renal tumor in the surrounding tissues. There is a case of retroperitoneal mass in my series in which an exploratory operation was performed and material for biopsy taken from the mass, which proved to be adenocarcinoma; at necropsy the primary growth was observed in the kidney. It is well to mention that a thorough search for metastasis must be undertaken; the lungs are the most frequent site for metastasis and the osseous system a less frequent site.

Relative to the routine use of intravenous urography in the diagnosis of abdominal conditions, it is well to bear in mind that negative evidence in the excretory urograms does not necessarily mean that the kidneys are not the seat of any lesion. A case in my necropsy series illustrates this fact very strikingly. The urinary tract was ruled out by intravenous urography. The complaints of the patient were referred to the gastro-intestinal tract, and there were general weakness and toxemia. The autopsy disclosed an adenocarcinoma of the right kidney. There were no metastases. Gastro-intestinal symptoms without accompanying urinary symptoms but with generalized weakness, loss of weight and negative results of x-ray examination

of the gastro-intestinal tract should impress the attending physician with the necessity of investigation of the urinary tract. Certain patients apparently are in good health but have vague gastric symptoms or discomfort in the right upper abdominal quadrant. They are usually studied from the point of view of the general surgeon or the gastro-enterologist. Two patients in my series who were under observation five years and two years, respectively, illustrate this point. Repeated cholecystograms and gastro-intestinal studies revealed nothing of note. It was not until the urinary tract was investigated that the correct diagnosis of renal neoplasm was made.

TABLE 5.—*Operative Approach*

	Number	Percentage
Lumbar (supplemented by resection of the twelfth rib in 16 cases)	36	63.15
Transperitoneal	18	31.57
Combined lumbar and transperitoneal	3	5.26
Irradiation		
Preoperative and postoperative irradiation	7	12.28
Postoperative irradiation	31	54.38
Irradiation alone	14	14.73

TREATMENT

The management of renal neoplasm has today resolved itself into three major groupings: first, preoperative and postoperative irradiation with surgical intervention; second, operation with subsequent irradiation, and, third, irradiation alone, used only when operation is contraindicated.

Waters'[2] recent paper on preoperative irradiation of cortical renal tumors is undoubtedly a valuable contribution to the modern management of the great majority of renal neoplasms. He noted a striking reduction in size of radiosensitive renal tumors following irradiation and has rendered operable tumors which were inoperable because of their large size. One must decide the type of tumor which is radiosensitive or radioresistant. Waters has shown that the radiosensitive type is the adenocarcinoma, or the so-called hypernephroma. Papillary carcinomas of the renal pelvis and malignant papillary cystadenomas are radioresistant. Such tumors are apt to metastasize by way of the ureter into the bladder, and therefore, if surgical procedure is decided on, a nephro-ureterectomy should be performed rather than a nephrectomy.

In my series seven patients (12.28 per cent) received both preoperative and postoperative irradiation; in two cases the preoperative irradiation was employed because of the size of the tumor, and after reduction in size of the tumor nephrectomy was performed. In thirty-one cases (54.38 per cent) postoperative irradiation was used.

In exposure of the kidney the surgeon has the choice of the lumbar route (the retroperitoneal) or the abdominal route (the transperitoneal) or a combination of the two. In thirty-six (63.15 per cent) of my cases the lumbar incision was employed; in eighteen (31.57 per cent) recourse was had to the transperitoneal route. The fact that the majority of surgeons prefer the transperitoneal approach in surgical treatment of tumor of the kidney does not necessarily mean that it is the only avenue of choice. The main reasons for the transperitoneal approach were invariably the size of the tumor and the comparative ease with which the pedicle could be efficiently controlled. Since preoperative irradiation will reduce the size of many renal neoplasms, the balance may be swung toward the lumbar route. Recourse to the combined method was necessitated in three of the cases in this series; in all the pedicle was large, short, adherent and so involved by adhesions that a transperitoneal approach supplemented the lumbar route. My feeling is that the lumbar route is the better, but when the operator is clinically assured that the pedicle presents technical difficulties of attack that will enhance the danger of hemorrhage the transperitoneal route becomes the avenue of choice. Difficulty in nephrectomy by the lumbar route presents itself when the tumor is so large that the surgeon cannot place the pedicle clamps efficiently. In sixteen cases the lumbar incision was supplemented by resection of the twelfth rib. Many surgeons advise this procedure in nephrectomy not only for neoplasms but for other renal lesions in which the kidney is adherent to the dome of the diaphragm, the liver and the retroperitoneum.

The dangers of biopsy in the case of renal neoplasm should be thoroughly appreciated; if there is any avenue for metastasis this certainly is one. I have had no personal experience with aspiration biopsy of renal neoplasms, but it seems to me that sound surgical philosophy is against this unsurgical procedure.

PROGNOSIS

The variable factors in the prognosis of renal neoplasm are notable in that there is a general lack of agreement among numerous writers. In reviewing this series of cases it becomes evident to me that several patients were subjected to nephrectomy for whom the prognosis was definitely poor. One patient already had metastasis to the lungs. The tumor was removed, and it was hoped to control the metastasis by irradiation to the lungs; the patient did not survive the operation. In this type of case the advisability of operation is questionable. Three additional postoperative deaths were noted in patients who gave a relatively short clinical history and had a large fixed tumor removed at operation. Apparently there were no local metastases; nevertheless, marked toxemia developed and death followed. Operation in this type of case seems inadvisable, and irradiation should possibly be recommended. The factors that must be taken into consideration to establish a favorable prognosis are: first, complete familiarity with the clinical history and physical status of the patient; second, the presence or absence of demonstrable metastases; third, the advisability of instituting preoperative irradiation; fourth, the chances of the patient to survive the ordeal of the operation; fifth, the type of neoplasm that is found and the

TABLE 6.—*Duration of Life After Operation (Nephrectomy Thirty-Four and Nephro-Ureterectomy Two)*

Duration, Years	Number	Percentage	Age at Death, Years
Less than 1	8	14.03	40, 43, 47, 50, 52, 56, 65, 76, including 6 postoperative deaths
1-2	8	14.03	36, 45, 49, 54, 57, 60, 63, 67
2-3	5	8.77	27, 41, 47, 59, 64
3-4	4	7.01	28, 45, 53, 62
4-5	3	5.26	56, 60, 61
5-6	3	5.26	57, 60, 66
6-7	2	3.50	56, 70
7-8	1	1.75	59
8-9	1	1.75	64
10 plus	1	1.75	63

	Under Five Years, Percentage	Over Five Years, Percentage
Survived	49.12	14.03

presence or absence of metastasis into or surrounding the pedicle or even the extracapsular and retroperitoneal tissues; sixth, the advisability of instituting postoperative irradiation, not only to the renal area but also to the lungs, as a prophylactic measure; seventh, the institution of general measures to fortify the patient against toxemia and anemia, and eighth, the constant observation of the patient because of the possibility of impending metastasis.

In the presence of metastasis operation should not be recommended unless the patient is in excellent physical condition and the surgeon is prepared to offer him the benefits of a complete radiologic service; it is a fact that the results of surgical intervention in this type of case are abominably poor.

It is wise to take into consideration the report of the pathologist before indicating a favorable prognosis. The histologic evidence of the grade of malignancy influences the prognosis. Involvement of the renal vein does not necessarily indicate an unfavorable prognosis. In one of my cases there was a large tumor thrombosis of the left renal vein at operation, but no evidence of distant metastasis could be found. This patient had a recurrence five years later in the left scrotal veins and epididymis, which were removed. He is living and well thirteen years after the removal of the kidney. Several patients have been observed at necropsy with large renal tumors in which the renal vein and vena cava were involved, but with only a few small, distant metastases, which apparently were very recent. On the other hand, there were cases in which no pedicular involvement was noted and the patient died within several years after the operation. Calcification of renal tumors is rather frequent and indicates a favorable prognosis. Local extension into the surrounding tissues also influences the prognosis. However, one patient in whom local extension was demonstrated is living and well today, two and one-half years after nephrectomy. He received irradiation postoperatively, as have the majority of patients since 1925.

In the operative series the highest percentage of mortality is in the first two years after operation. The contributing factors that influence this high mortality are the development of metastasis and subsequent profound toxemia. Some of the patients may be salvaged in the future by the application of the more modern methods of management, particularly in regard to irradiation, preoperative and postoperative.

TABLE 7.—*Data on Fifteen Patients Who Had Nephrectomies and on Two Who had Nephro-Ureterectomies*

Name	Age	Sex	Date	Pathology	Metastasis	Roentgen Treatment	Living After	
							Years	Months
G. McB.	54	♂	2/ 8/24 12/11/29	Left adenocarcinoma Carcinoma, left epididymis	..... Yes	Postoperative	13	3
L. S.	42	♂	11/ 3/27	Right adenocarcinoma	None	Postoperative	9	6
G. M.	53	♂	11/14/28	Right adenocarcinoma	None	Postoperative	8	6
H. C.	53	♀	5/20/30	Right carcinoma	None	Postoperative	7	
E. B.	49	♀	5/31/30	Right adenocarcinoma	None	Postoperative	7	
J. K.	47	♂	7/11/30	Right adenocarcinoma	None	Postoperative	6	10
A. W.	57	♀	11/28/30	Right adenocarcinoma	None	Postoperative	6	6
E. H.	7 months	♀	9/ 9/32	Left embryonal carcinoma	None	Preoperative and postoperative	4	8
B. F.	47	♂	4/11/34	Right adenocarcinoma	None	Preoperative and postoperative	3	1
H. P.	49	♀	5/31/34	Right adenocarcinoma	None	Postoperative	3	
C. M.	49	♂	7/ 3/34	Right adenocarcinoma	None	Postoperative	2	10
J. L.	54	♂	9/ 9/34	Right adenocarcinoma; involvement of renal vein and capsule	None	Preoperative and postoperative	2	8
J. T.	54	♂	1/31/35	Left adenocarcinoma	Yes	Postoperative	2	4
A. S.	43	♀	5/ 4/36	Right adenocarcinoma	None	Preoperative and postoperative	1	
H. B.	45	♂	7/22/36	Right adenocarcinoma	Yes	Preoperative and postoperative	0	10
M. M.	6	♀	9/14/36	Embryonal carcinoma, Wilms tumor	None	Preoperative and postoperative	0	8
L. S.	46	♂	12/11/36	Left papillary adenocarcinoma	None	Postoperative	0	5

Seventeen living (29.82 per cent); seven living after five years (12.28 per cent); six living after from two to five years (10.52 per cent).

COMMENT

The follow-up studies in this series of cases were undertaken seven years ago. The results may seem disappointing. The crying need for more thorough observation on the part of the physician is evident. If every effort was made to eliminate the possibility of renal tumor in cases of hematuria, the outlook following their surgical removal would be more favorable.

The variations in the clinical picture and, in conjunction, the histologic examination of the neoplasm, with or without metastasis, are the practical problems that must be considered in attempting to establish a favorable prognosis.

Waters [2] and Wharton [6] have reported interesting results of preoperative irradiation. The number in our series who received preoperative irradiation is small, seven (12.28 per cent). The duration of life following this treatment is not sufficient to warrant any comment at the present time. The majority of patients in my series received irradiation postoperatively. At present one cannot tell what the final outcome will be in comparison with that of preoperative irradiation. Whether or not metastasis is prevented or controlled is questionable, as the metastasis, although undemonstrable, may have been present before the patient was treated.

There should no longer be any question of the advisability of instituting irradiation in the treatment of large renal tumors before surgical intervention is attempted. In so doing one must remember that operative removal is imperative from three to five weeks after the irradiation, as regrowth is likely to occur if operation is delayed too long. One is compelled to doubt the few reports that are available wherein postoperative irradiation is said to have cleared up the metastasis. In several cases in my series, metastasis to the lungs was definitely controlled temporarily, but the patient died from a year and a half to two years after the discovery of the metastasis.

The percentage of patients living over five years is 26.28 (tables 6 and 7). The highest mortality rate occurred within the first two year period (in our series 28 per cent). Metastases, as noted previously, can occur early or late. The majority, however, appear to develop relatively early, possibly within the first two years, and thus death is merely a matter of time.

6. Wharton, Lawrence R.: Preoperative Irradiation of Massive Tumors of the Kidney: A Clinical and Pathologic Study, Arch. Surg. **30**: 35-51 (Jan.) 1935.

SUMMARY

Of ninety-five patients with renal carcinoma, fifty-eight (61 per cent) were subjected to operation, of which number seventeen (29.82 per cent) are living after from five months to thirteen years and three months; thirty-six (63.15 per cent) are dead, including six (0.52 per cent) who died after operation. The survival period of the remaining thirty (31.57 per cent) was from less than one year to ten years and five months. Four patients (7.01 per cent) were not traceable. Thirty-one (32.63 per cent) of the ninety-five were studied at necropsy. In seventeen (17.89 per cent) of these the condition was a chance observation; ten (10.43 per cent) died after irradiation, as their carcinoma was considered inoperable, and four (6.31 per cent) died after operation. Metastasis was found most frequently in the lungs, liver, adrenals and osseous system and less frequently in the lymph glands, renal vein, inferior vena cava, kidney, spleen, heart and brain.

Eleven patients (11.57 per cent) received no treatment, for various reasons.

Renal neoplasms are considered to be renal carcinomas in that true columnar epithelial cells forming definite acini and papillae may be demonstrated. The term hypernephroma is used only to refer to definite adrenal tissue tumors.

This study should impress all clinicians with the importance of the variability of the symptom complex of renal neoplasm. When the so-called four cardinal signs and symptoms of renal tumor (hematuria, pain, mass and a typical pyelographic defect) are present, the diagnosis is simple. Pyeloscopy is a distinct aid in the differential diagnosis of renal lesions. It is important to emphasize the necessity for more investigation on the variable nature or type of renal neoplasms, so that urologists will be able to recommend sound, logical treatment.

The surgical approach to the kidney should depend on the individual conditions and the surgeon's judgment. With the important adjunct of preoperative irradiation, many renal tumors decrease in size, so the lumbar route may be employed more frequently in the future than it has been in the past. For many years in Jefferson Hospital the lumbar incision was supplemented by resection of the twelfth rib. However, the transperitoneal approach still serves as the avenue of choice in many clinics.

With the use of preoperative irradiation as an adjunct to surgical intervention, I believe a distinct advance has been made in the practical management of renal neoplasm. The results reported in the literature hold forth much promise. Nevertheless, the use of postoperative irradiation must be continued in many cases. I am convinced that routine postoperative irradiation has extended the survival period of many of my patients. In view of this experience I shall continue to recommend it.

The prognosis of renal neoplasm places the urologist in an unenvied position. It has been noted that extension of the carcinoma to the renal vein does not necessarily mean a poor prognosis and, vice versa, that no metastasis found in the renal vein at the time of operation does not indicate a favorable prognosis. It is important to remember in this regard that the histologic characteristics of the tumor and, less frequently, the gross appearance of the neoplasm, together with a complete familiarity with the clinical history and physical condition of the patient, will often help in building up a favorable or unfavorable hypothesis as to the probable survival period. I have definite evidence from both autopsies and operations that metastases do not necessarily occur early. In many cases even though the tumor in the kidney was very large no evidence of metastases could be demonstrated.

Lastly, let me stress the need for individualization in each case of suspected renal neoplasm, in diagnosis, treatment and future observation.

255 South Seventeenth Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. KREUTZMANN AND COLLOFF, DRS. HINMAN AND POWELL AND DR. FETTER

DR. JAMES L. ESTES, Tampa, Fla.: Drs. Hinman and Powell have shown the recent advances in the management, diagnosis and prognosis of tumor of the testes and have presented a paper that should be appreciated by urologists and general practitioners alike. The diagnosis, management and prognosis of carcinoma of the bladder took a long jump forward when the Carcinoma Registry of the American Urological Association was formed, and the work of the committee and its contributors has been of inestimable value to urologists in the management of such cases. Those engaged in teaching are stressing more and more the importance of the early diagnosis of cancer and impressing on the minds of students the significance of hematuria. It is my feeling that whenever possible, before lay bodies or doctors, urologists should place great emphasis on the passing of blood from the bladder. It should not be difficult to diagnose tumors of the bladder, provided a complete urologic survey is made. It is not always easy to determine the exact extent of infiltrating tumors, and these are the ones that require accurate precision in selecting the best method of procedure. Paring down by transurethral resection and fulguration with postoperative irradiation certainly seems the method of choice, but through the opened bladder and by careful palpation with a finger in the rectum (if necessary) the surgeon can define more clearly the local extent and destroy more of the tumor. Certainly radon seeds can be more accurately placed. The urologist must have the thorough cooperation of a clinical pathologist and roentgen therapist in dealing with tumors of the bladder. It is my opinion that preoperative irradiation has been of much help in dealing with carcinoma of the bladder. In metastasis and preventing recurrence, it has a definite place and is the urologist's chief source of therapy. The development of the supervoltage machine used both before and after operation gives more hope than ever that the patient presenting himself with carcinoma of the bladder can be offered better end results than heretofore. As in carcinoma of the bladder, hematuria and pain constitute the outstanding symptom in renal carcinoma and it is my opinion that the average practicing physician is not aware of the possibilities of kidney tumor as he is of bladder tumor. A thorough study during the time of bleeding will reveal evidence of the source and cause of bleeding much more readily than when the examination has been deferred until bleeding has stopped. This, I think, urologists should keep before the minds of those engaged in general practice. When hematuria is present, one should make a thorough study from the meatus to the cortex, as well as search for metastasis.

DR. RUSSELL S. FERGUSON, New York: We are indebted to Drs. Hinman and Powell for their presentation of the management of the patient with teratoma testis. They have presented an orderly routine for the diagnosis and treatment of these highly malignant tumors. It is gratifying to hear again confirmation of the original observations of the behavior of gonadotropic substance in teratoma testis, namely, that the amount excreted varies in proportion to the embryonal character of the neoplasm and to the mass of tumor, and, further, that the variation in excretion following irradiation of the tumor is of prognostic importance. All urologists are agreed that the failure of the hormone to diminish after irradiation is a fatal

prognostic sign, whereas when the amount of gonadotropic substance excreted diminishes rapidly in response to irradiation the prognosis is favorable. The failure to find a measurable amount of hormone in some of the more adult types of tumors is probably not because of the absence of the hormone but because of the crudeness of our biologic tests, which fail to detect the small amounts that are almost certainly present. Negative results, therefore, in this group of cases with present technic are not significant. Positive results are always significant. I find myself in disagreement with Drs. Hinman and Powell on the point of orchidectomy before irradiation. It is conceded that the scientific information to be obtained by microscopic examination of the unaltered tumor and the assay of fresh tissue for gonadotropic substance is an advantage. However, this advantage carries little weight when it is seen that the clinical results to be obtained at the end of five years are better when irradiation precedes orchidectomy. In a review of the Memorial Hospital series of 292 teratomas of the testis treated between 1917 and 1929, it was found that of fourteen patients with primary operable tumors treated by irradiation before orchidectomy, eleven, or 78.5 per cent, were alive and without evidence of disease at the end of five years, whereas of twenty-eight patients with primary operable tumors subjected to orchidectomy before irradiation only twelve, or 42.8 per cent, were alive and well without evidence of disease at the end of five years. It is granted that this spread in results in favor of irradiation before orchidectomy might not be as great had irradiation of all the patients who underwent orchidectomy been done first without delay. In some instances there was considerable delay between the orchidectomy and the irradiation, and therein lies the danger of advising orchidectomy before irradiation. While Drs. Hinman and Powell would not countenance delay, many surgeons are inclined to put off irradiation after orchidectomy until other symptoms ensue. Then it is often too late. It is possible that with immediate irradiation after orchidectomy there may be no difference in the five year end results as compared with patients irradiated before orchidectomy. Yet for the present I feel that the advantage lies with preoperative irradiation.

DR. ALFRED F. HOCKER, New York: Dr. Fetter has made clear the pathologic classification of renal tumors and has stressed the importance of thorough urologic examination whenever hematuria is present. I was impressed by the meticulous examination which he makes, and especially by his use of pyeloscopy as well as the usual pyelography in radiologic studies of the kidney. Dr. Fetter states that aspiration biopsy is unsurgical. With this I disagree. I have employed aspiration biopsy in a number of cases and have never found it to cause any ill effects on the tumor. Dr. Stewart of the Memorial Hospital has examined more than 7,000 aspirations and has never noticed any damaging effects from its use. Certainly no one objects to the curettage of a cancerous uterus for the diagnosis of neoplasm of the organ nor does the surgeon consider this procedure unsurgical. Regarding the roentgen therapy of renal neoplasms I agree with the criteria of Dr. Fetter. All bulky adult carcinomas of the kidney receive a prolonged preoperative course of daily fractionated doses of x-rays. I have found that it reduces the size of the tumor and makes the operation easier for the surgeon and less hazardous for the patient. I believe that this regression, however, is not due to the radiosensitivity of the cancer but rather to the secondary circulatory accidents which occur; that is, the increase in the number of infarcts in the kidney. Besides reducing the size of the tumor, radiation therapy undoubtedly lessens the toxemia and by allaying hemorrhage counteracts the anemia. I feel that all adult renal carcinomas are radioresistant. If any are radiosensitive, I believe that they are papillary carcinomas of the renal pelvis. After a full course of roentgen therapy to the bulky carcinomas, a nephrectomy is done six weeks after the last treatment, depending, of course, on whether or not distant metastasis is present. Embryonal carcinomas in infants are the only type which I have been able to sterilize by x-rays, and in these I rely on irradiation alone or irradiation plus surgical intervention.

DR. LLOYD G. LEWIS, Baltimore: With the development of transurethral surgery, urologists may have acquired a rather casual reaction toward cancer. Not many apparently have any established idea of the curability of carcinoma of the prostate or bladder. Yet it is their duty to institute treatment toward that end. Palliation is acceptable only when cure is impossible. Noninfiltrating bladder tumors can be eradicated by transurethral surgery plus radium. But there is no proved substitute for radical operation in the treatment of operable infiltrating tumors of the bladder and prostatic carcinoma. The excellent papers of this symposium serve to clarify our position. Agreeing with Drs. Hinman and Powell, I can see no logic in preoperative irradiation of testicular tumors. They can be easily and completely removed without operative traumatism. On the other hand I am convinced of the advisability of preoperative irradiation of cortical renal and perirenal tumors. I think that the first paper on preoperative irradiation of renal tumors was written by Drs. Waters, Frontz and myself in 1933 (Radiation Therapy of Renal Cortical Neoplasms with Special Reference to Preoperative Irradiation, *South. M. J.* **27**:290 [April] 1934). One of the most thrilling experiences in my urologic career occurred recently when I reexamined a patient operated on seventeen years ago for carcinoma of the prostate by Dr. Young. The diagnosis was established pathologically. There was no palpable evidence of recurrence and roentgenograms were negative for metastasis. May I express my profound admiration for and devotion to the man who taught many of us the perineal route to the prostate, seminal vesicles and bladder. To illustrate the perineal approach for bladder tumor, Dr. Young has asked me to present his case. A man, aged 42, came to the Brady Urological Institute, complaining of intermittent hematuria of two years' duration. The tentative diagnosis of carcinoma of the prostate was made by rectal examination. Because of the limitation of the tumor within the prostatic capsule, radical removal was considered possible. Instrumentation was impossible owing to obstruction in the prostatic urethra. When the prostate was exposed the induration was less evident, and frozen sections from the posterior lamella were negative for carcinoma. Dr. Young then performed urethrotomy and obtained a specimen from the vesical orifice, using his punch. These sections showed transitional cell tumor. The bladder was opened anteriorly, as in the radical operation for carcinoma of the prostate. Digital examination revealed a tumor involving the vesical orifice and right side of the bladder. Resection of the entire prostate and right side of the bladder was carried out. Closure was similar to that in radical perineal prostatectomy.

DR. V. D. LESPINASSE, Chicago: The urologic cancer problem is no different from the cancer problem in relation to any other group of organs or any other group of individuals. Most of the discussion today has been on the technical procedures and treatment. I think there should be some methods or means taken so that these cases will get to us earlier. One of the deficiencies of urologic work is that we do not get these cases early enough. Why don't we get these cases earlier? There are two reasons. First, urologic carcinomas are asymptomatic; they cause the patient very little or no pain. If one is keen and can get to examine the patient on one of his routine birthday examinations one can detect carcinoma by putting the finger in the rectum and palpating the prostate. In the urine, one may see an increase in epithelial cells or occasionally a few red blood cells. If these conditions are found, one should have the courage to insist that the patient submit, without delay, to a complete urologic examination, including cystoscopy and roentgenology. The number of cases of carcinoma that will be obtained in this way are relatively few. The second circumstance that brings the patient to the urologist is the sign hematuria. These patients wake up in the morning, urinate, and see a red, brown or black fluid issuing forth. Immediately they go to the telephone and call the doctor, but the doctor is not there. They fuss around a little bit, urinate again, and find the good old yellow color back again. At once they forget the doctor and go about their affairs. Then, in six months or a year, they have a recurrence of their hematuria, and they appear for a urologic examination. I feel that urologists should stress the point in all their contacts with medical colleagues and medical students that hematuria, no matter how slight or how soon stopped, calls for a complete urologic examination.

DR. FRANK HINMAN, San Francisco: I wish to reopen the controversy of transurethral resection and perineal prostatectomy. I think it is proper in view of Dr. Lewis's remarks. The reason that I wish to do this is that I think the point of Dr. Young's paper has been entirely overlooked. Hyperplasia of the prostate does not always occur as an isolated condition, and any method of treatment which always treats it as an isolated condition does not conform to the highest standard of cure. We know that infections in the prostate, stones of the prostate, and carcinoma of the prostate are frequently associated with hyperplasia. Carcinoma occurs in two forms: primary carcinoma in the posterior lobe and primary carcinoma that occurs in the hyperplasia itself. In a recent paper, a histologic study by Heyntschak in Vienna showed that 3 per cent of the prostates removed by suprapubic prostatectomy had carcinoma in them unsuspected. These patients before operation presumably were all cured by removal of this hyperplasia. It seems to me that the matter has degenerated into more or less of a question of choice of the operator himself. Perineal prostatectomy not only conserves in certain cases the sexual function and not only restores the ability to urinate normally but it gives an opportunity to treat these associated conditions, and particularly the carcinoma. The perineal route is the only method by which one can radically remove carcinoma of the prostate; the perineal route is the only method by which stones can be radically removed, and therefore, in a consideration of the standard of cure, a method that does not take into consideration this association does not conform to the highest standard of cure.

QUININE IN MYOTONIA AND PROSTIGMINE IN MYASTHENIA

A CLINICAL EVALUATION

FOSTER KENNEDY, M.D., F.R.S. (EDIN.)
AND
ALEXANDER WOLF, M.D.
NEW YORK

With Walker's [1] discovery that prostigmine alleviates the muscular weakness of myasthenia gravis and Wolf's [2] finding that quinine abolishes the myotonus of congenital and atrophic myotonia, new impetus was given to the study of the pathophysiology of these disorders. The clinical observation [3] that prostigmine exaggerates myotonia and that quinine exaggerates myasthenia established a relationship of opposition in response to drugs that accentuated the obvious contrast between these muscular states. It is this contrast that makes appropriate a comparative evaluation of their symptomatic response to pharmacologic antagonists.

It is two years since Walker's [1] contribution and one year since Wolf [2] suggested the use of quinine, so that an appraisal of the clinical usefulness of prostigmine and quinine is due. In this period we have studied, seen or been in indirect contact with nine patients with myasthenia gravis, nine patients with myotonia congenita and eighteen patients with myotonia atrophica.

Every patient with myasthenia gravis showed an immediate excellent response to prostigmine, with generalized increase in muscular power. Patients previously bedridden and gasping for breath became ambulatory and took light exercise. However, within one to four months four patients began to show a progressively poorer response to prostigmine, so that the dose had to be increased gradually to maintain swallowing and aid respiration. In spite of increases in medication of from two to ten, fifteen and even twenty-four ampules (0.5 mg. per ampule) in twenty-four hours, these patients were at times almost at the point of death. Even with these high doses no painful peristalsis occurred. Sweating, however, was marked in all cases. It semed that, if prostigmine was given beyond a certain point, patients became refractory toward its beneficial effects. Yet if insufficient prostigmine was given, respiration became labored and swallowing impossible. Accordingly, the administration of prostigmine was discontinued for from thirty-six to forty-eight hours, during which time the administration of potassium chloride and ephedrine sulfate was pushed to a point just below intolerance. Orders were left to institute artificial respiration and to give prostigmine in case of emergency. Swallowing became impossible, so that feeding by tube was required. After from thirty-six to forty-eight hours prostigmine medication was resumed in one case with one ampule (0.5 mg.) twice a day. This patient showed a much better response to two ampules after a two day abstinence than she previously had to twenty-four ampules. Gradually, however, her medication has had to be increased to twelve ampules a day, and again she is much less responsive. A second patient, formerly given from eighteen to twenty-four ampules, has maintained a fair degree of strength while receiving four ampules a day after a two day abstinence. A third patient was formerly given from eighteen to twenty-four ampules, despite which swallowing remained impossible. He has had no prostigmine now for four months and shows few signs of deprivation. He may be in a state of spontaneous remission. The dosage in the fourth case has not yet been reduced.

Why certain of our patients should after a while become refractory to prostigmine is not clear; nor can we be certain that the patients who have responded well so far will not at some time become refractory. In theoretical explanation it could be postulated that choline esterase keeps increasing in the blood, requiring constantly higher concentrations of prostigmine. This notion is difficult to maintain in the light of contradictory reports on the blood choline esterase in patients with myasthenia gravis. Stedman [4] obtained low values. McGeorge [5] reported three cases of myasthenia gravis in which the activity of the serum esterase was well within normal limits and showed little variation from day to day. However, Brown, Dale and Feldberg [6] have stressed the importance of the local concentration of acetylcholine at the end-plate. One can imagine the concentration of choline esterase at the myoneural junction as excessive, a state unrevealed by study of the blood. Another possibility is the periodic exhaustion of acetylcholine at the end-plate. At such times it would not matter how strongly esterase was inhibited by any quantity of prostigmine. A key to this problem may lie in Boothby's [7] clinical observation, and we can

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1. Walker, Mary: Case Showing Effect of Prostigmin on Myasthenia Gravis, Proc. Roy. Soc. Med. **28**: 759-761 (April) 1935.
2. Wolf, Alexander: Quinine: An Effective Form of Treatment for Myotonia, Arch. Neurol. & Psychiat. **36**: 382-383 (Aug.) 1936.
3. Kennedy, Foster, and Wolf, Alexander: Experiments with Quinine and Prostigmin in Treatment of Myotonia and Myasthenia, Arch. Neurol. & Psychiat. **37**: 68-74 (Jan.) 1937.
4. Stedman, Edgar: The Choline Esterase Content of Blood in Myasthenia Gravis, J. Physiol. **84**: 56*P* (July) 1935.
5. McGeorge, Murray: Choline Esterase Activity in Disease with Special Reference to Myasthenia Gravis, Lancet **1**: 69-72 (Jan. 9) 1937.
6. Brown, G. L.; Dale, H. H., and Feldberg, W.: Reactions of Normal Mammalian Muscle to Acetylcholine and to Eserine, J. Physiol. **87**: 394-424 (Sept. 8) 1936.
7. Boothby, W. M.: Myasthenia Gravis, Ann. Int. Med. **9**: 143-149 (Aug.) 1935.

confirm this, that there is a definite correlation between the patient's general condition and the amount of dry, stringy oral mucus. The production of this mucus is more marked when the patient is worse. It appears to us that this dry, viscous mucus makes its appearance only when there is inadequate flowing salivation. Stavraky [8] quotes an experiment by Heidenhain,[9] in which he paralyzed the secretory effects of the chorda tympani with quinine although the sympathetic nerve still acted. It follows that the vagus hormone or parasympathetic stimulation produces watery salivation and that in extreme myasthenic states there is a deficiency of acetylcholine resulting in inadequate salivation and dry oral mucus. Yet the supposition of myoneural acetylcholine insufficiency wears thin under the experimental observation that acetylcholine or acetyl-beta-methylcholine administered at such times does not increase muscular power.

The refractory character of prostigmine after an early extended period of usefulness has been noted by other investigators. Minski and Stokes [10] noted immediate toxic symptoms, alimentary, cardiovascular and nervous, causing complete prostration. We have not seen such symptoms except after prolonged and excessive medication. But Minski and Stokes stated that it is hopeless to undertake continuous treatment with prostigmine outside the hospital. They confirmed the remarkable specific effect of prostigmine but said its usefulness is limited. We, however, have been able to administer prostigmine hypodermically or orally to four patients outside the hospital for many months. Hyland [11] pointed out the dramatic but transient relief from symptoms in four patients and warned against repeated administration on the grounds that it may be followed by alarmingly increased weakness. He admitted, however, that there are several cases on record in which rather large doses were given every day without ill effect. Boothby [12] has emphasized that treatment with prostigmine may be followed by mental depression and greater weakness after early improvement. C. K. Russel [13] described his experience with a case of myasthenia gravis: "It was disappointing that, while the effect lasted for four or five hours, there resulted what seemed to be a decided let-down, and he was not nearly so well after the injection; so I felt hesitant about repeating it more often than was necessary. I had to put him in the Drinker respirator, and the use of the respirator and the drug was continued for several days, but he finally died. The let-down about five or six hours after the administration of the prostigmine seemed to me a serious disadvantage." Harvey and Whitehill,[14] while granting that prostigmine produces striking immediate improvement and seems at present to be the most valuable therapeutic agent, described three patients in whom beneficial effects decreased with the continued use of the drug until they died. Another patient never became able to walk about in spite of 15 mg. nine or ten times a day. In a fifth patient, although prostigmine, 30 mg. three times a day, helped chewing, swallowing and diplopia, its effects wore off in from two to three hours, and the patient thought his muscular weakness was worse than before the drug was taken.

It is our belief that prostigmine given in doses of from 15 to 30 mg. two or three times a day may be life saving, but if given over a considerable period in excess of this dosage or over too long a time in this low dosage, it may become intoxicating and result in death. Prostigmine facilitates the action of acetylcholine and so stimulates the voluntary muscles via the myoneural junction, but in large doses it appears to exert a curare-like effect, which very likely results in weakness, then paralysis and finally death, when the respiratory muscles become affected. The optimum dose must lie in the marginal safety zone between prostigmine stimulation and prostigmine "curarization" of the motor end-plate. This dose varies for each patient.

Our experience with quinine in the treatment of myotonus extends over six cases of myotonia congenita and fifteen cases of myotonia atrophica for a period of one year. In addition we know through personal communication from a physician in another hospital of three cases of myotonia atrophica. Smith [15] has recently reported three cases of myotonia congenita the symptoms of which were entirely abolished by quinine. In each patient of our series from 2½ to 5, 10 or 15 grains (0.16 to 0.32, 0.64 or 0.96 Gm.) of quinine hydrochloride by mouth two or three times a day eliminated every vestige of myotonus. Any form of quinine may be used; for example, hydrochloride, sulfate, bisulfate or hydrobromide. Of the group, however, the hydrochloride appears to be the most soluble and quickly absorbed without disturbing gastro-intestinal effects. The hydrobromide may be used with "nervous" patients.

An explanation of the continuous neutralization of myotonus lies in the maintenance of an almost constant level of quinine after it is administered by mouth.[16] The drug can be detected in the blood for about twenty-five hours, a good deal longer than if given intravenously. The blood quinine content does not rise above 3 per cent of the dose given. Hartmann and Zila [17] demonstrated that after intravenous injection of 0.5 Gm. of quinine the concentration in the blood fell quickly at first, then steadily more slowly, until after eight hours none was left. When quinine was taken by mouth the blood quinine content was lower but was nearly constant for about twenty-four hours. Quinine is absorbed slowly. Part of it circulates in the blood before excretion unchanged in the urine. About one third is excreted within twenty-four hours.[18] The remainder is destroyed by the body metabolism.[19] In only one patient (J. P.) was there a sign of cinchonism, evidenced by ringing in the ears. This occurred when she took 10 grains (0.64 Gm.) of quinine hydrochloride three times a day by mouth. Doses of 5 grains (0.32

8. Stavraky, G. W.: Effect of Quinine on the Parasympathetic and Sympathetic Innervation of the Salivary Glands, J. Pharmacol. & Exper. Therap. **47**: 321-338 (March) 1933.
9. Heidenhain, R.: Stud. d. Physiol. Inst. zu Breslau **4**: 85, 1868.
10. Minski, Louis, and Stokes, A. B.: Treatment of Myasthenia Gravis, Brit. M. J. **1**: 1095-1098 (May 30) 1936.
11. Hyland, H. H.: Treatment of Myasthenia Gravis, Canad. M. A. J. **35**: 372-381 (Oct.) 1936.
12. Boothby, W. M.: Myasthenia Gravis: Eighth Report, Tr. A. Am. Physicians **51**: 188-198, 1936.
13. Russel, C. K., in discussion of Winkelman, N. W., and Moore, M. T.: Prostigmin in the Treatment of Myasthenia Gravis and Muscular Dystrophy, Arch. Neurol. & Psychiat. **37**: 237-252 (Feb.) 1937.
14. Harvey, A. M., and Whitehill, M. R.: Prostigmin as an Aid in the Diagnosis of Myasthenia Gravis, J. A. M. A. **108**: 1329-1333 (April 17) 1937.
15. Smith, W. A.: Quinine Treatment of Myotonia Congenita, J. A. M. A. **108**: 43 (Jan. 2) 1937.
16. Meyer, H. H., and Gottlieb, R.: Experimental Pharmacology as a Basis for Therapeutics, translated by V. E. Henderson, Philadelphia, J. B. Lippincott Company, 1926, p. 561.
17. Hartmann, H., and Zila, L.: Ueber die sogenannte Chiningewöhnung, München. med. Wchnschr. **64**: 1597, 1917.
18. Giemsa, G.: Ueber die therapeutische Verwertbarkeit der freien Chininbase, Arch. f. Schiffs- u. Tropen- Hyg. **11**: 300-302, 1907. Nishi, M.: Ueber eine neue Bestimmungsmethode des Chinins und über seine Ausscheidung im Harne, Arch. f. exper. Path. u. Pharmakol. **60**: 312-323, 1909.
19. Grosser, P.: Ueber das Verhalten des Chinins im Organismus, Biochem. Ztschr. **8**: 98-117, 1908.

Gm.) three times a day were well tolerated and adequate to eliminate symptoms.

In every case of myotonia congenita quinine proved to be of unique value. When administration of the drug was stopped, evidence of myotonia returned within twenty-four hours but was not complete before seventy-two hours. Patients consistently asked for quinine when it was not given, insisting on its beneficial subjective effect. The solution of myotonus was equally evident on objective examination, even to the dissolving of percussion myotonus in the voluntary muscles, including the tongue. In rare instances when myotonia was not evident on volition, a remnant of it could be elicited on percussion.

In cases of myotonia atrophica, although quinine readily neutralized myotonic reactions, it had less clinical usefulness. The reason for this is simple. The patient with the atrophic variety of myotonia is incapacitated much more by atrophy than by myotonus. In at least two or three patients the stage of myotonia had been outlived or had never developed. Yet there was no question that they belonged in this diagnostic class. Only three of eighteen patients with atrophic myotonia demanded to continue taking quinine, indicating a need and appreciation of the drug not evident in the others.

One man with myotonia congenita and one woman with myotonia atrophica appeared to have a slight decrease in myotonus for several weeks after they stopped taking the drug. The man had used quinine for ten months; the woman had used it for three months. Whether this partial release from myotonia will be transient or permanent remains to be seen.

In a previous paper we [3] reported the exaggeration of myotonia by prostigmine. We have since been able to confirm Russell and Stedman's [20] similar experience with potassium, which piles up more evidence for the brief of pharmacologic antagonism between myotonia and myasthenia. We have also confirmed Stedman's Scottish observation that alcohol given by mouth reduces myotonus considerably. Its sole disadvantage is of course chronic inebriation and the exciting to envy of less fortunate patients, not to speak of some damage to the discipline of the wards. Possibly, however, these by-products of this therapy would naturally attract little or no attention north of the Tweed.

We have been confronted with cases of supposed myotonia congenita in which the attending physician protested that quinine was ineffective. Careful examination showed the patients to be suffering from other disorders, such as hemiplegic spasticity or tetany. This led to an investigation of the effect of quinine and prostigmine on other neuromuscular disorders. Before recording our own experience we shall mention that of others. Everts [21] employed prostigmine in cases of myotonia congenita, alcoholic polyneuritis, postencephalitic parkinsonism, facioscapulohumeral myopathy and amyotrophic lateral sclerosis. Some improvement followed, but the patients were not treated regularly or for a sufficiently long period. It is curious to find that Everts noted improvement in patients with myotonia following the administration of prostigmine. We have given this drug many times in cases of myotonia and found the myotonus to be consistently exaggerated. Winkelman and Moore [22] reported two of four patients with pseudohypertrophic muscular dystrophy who improved after taking prostigmine, one with "muscular dystrophy" who responded favorably, and one with scapulohumeral muscular dystrophy (Erb) and one with amyotrophic lateral sclerosis who failed to improve. The majority of the patients with myasthenia gravis had received ephedrine or aminoacetic acid or both for an extended period without any appreciable improvement. Our experience with aminoacetic acid (glycine) in the treatment of myasthenia gravis has likewise been discouraging. Hamill and Walker [23] reported increased motor power in cases of amyotrophic lateral sclerosis following the use of moderate doses of prostigmine. Hurwitz and Gerstle [24] found no improvement in patients with amyotonia congenita after treatment with physostigmine and prostigmine.

We have used prostigmine and quinine in one case of chronic chorea, two of ordinary chorea, one of hemiathetosis, a dozen of spasticity associated with hemiplegia, one of tic involving the facial and cervical muscles, a dozen of chronic encephalitis, two of spasmodic torticollis, one of amyotonia congenita, two of progressive muscular dystrophy, one of Westphal's pseudosclerosis and one of ophthalmoplegia caused by botulism. One patient with the facioscapulohumeral myopathy of Laudouzy and Dejerine showed some slight subjective and objective improvement after taking 0.5 mg. of prostigmine subcutaneously three times a day. When this dose was given five times a day extreme weakness appeared, apparently a "curare" effect from excess prostigmine.

We [3] have reported elsewhere an experiment which indicates that the myotonic phenomenon is due to a pathophysiologic state resident in muscle or at the myoneural junction independent of the spinal neuronal reflex arc. Since myotonia and myasthenia appear to be counterparts responding to pharmacologic antagonists, and since myasthenia is conceived as a state in which there is excess choline esterase or inadequate acetylcholine at the motor end-plate, myotonic phenomena are in all likelihood due to an accumulation of acetylcholine or to an insufficient concentration of choline esterase at the motor end-plate. Yet it is difficult to imagine how myotonus could be due to excess acetylcholine, when atropine, an antagonist of acetylcholine, has little or no effect on the disease. Maybe the parasympathetic "stuff" at the motor end-plate or in muscle in this disease is somehow unaffected by atropine.

To test and confirm our notion of the localization of the pathophysiologic site in myotonia and myasthenia, 500 cc. of whole blood was transfused from a patient with myotonia congenita (J. D.) to a patient with myasthenia gravis (J. F.). Our feeling was that if these diseases were pathophysiologic opposites we might transfer parasympathetic "stuff" from the one to the other to produce a transient neutralization of myasthenic weakness and increase strength. The converse, in a sense, of this experiment, the transfusion of 500 cc. of whole blood from a normal individual (F. Q.) to a patient with myotonia congenita (J. D.), was also

20. Russell, W. R., and Stedman, Edgar: Observations on Myotonia, Lancet **2**: 742-743 (Sept. 26) 1936.

21. Everts, W. H.: The Treatment of Myasthenia Gravis by the Oral Administration of Prostigmine, Bull. Neurol. Inst. New York **4**: 523-530 (Dec.) 1935.

22. Winkelman, N. W., and Moore, M. T.: Prostigmin in the Treatment of Myasthenia Gravis, Arch. Neurol. & Psychiat. **37**: 237-252 (Feb.) 1937.

23. Hamill, P., and Walker, M. B.: The Action of "Prostigmin" (Roche) in Neuromuscular Disorders, J. Physiol. **84**: 36-37*P* (May 13) 1935.

24. Hurwitz, Samuel, and Gerstle, Mark, Jr.: Amyotonia Congenita with Familial Incidence, Arch. Neurol. & Psychiat. **33**: 1317-1323 (June) 1935.

performed but was not followed by diminished percussion or volitional myotonus. In the first procedure it was anticipated that the hypothetic excess of acetylcholine in the myotonic patient could be transferred to the myasthenic subject who suffered from a supposed lack of the vagus hormone. In the second experiment it was believed that the normal concentration of choline esterase in the blood of the unaffected individual might neutralize the "excess acetylcholine" in myotonia. No change in muscular symptoms was noted. This experiment confirmed our belief that the pathologic change of these disorders lies in muscle or at the myoneural junction. In a previous experiment we [3] established the innocence of the spinal reflex arc, and now the blood is seen not to carry the offending "stuff" in concentrations great enough to affect the disordered muscles or end-plates.

Dr. H. G. Wolff,[25] in order to ascertain whether the constriction of the pupil is due to action of acetylcholine, the radial muscle of the iris or parasympathetic nerve endings, allowed the postganglionic parasympathetic nerve fibers to degenerate after removal of the ciliary ganglion in three cats. Acetylcholine, injected into the anterior chamber of the eye, produced miosis. This experiment indicated "that, at least for the iris of the cat, the action of acetylcholine is peripheral to the postganglionic fibers and presumably direct on the radial muscles."

Elsewhere Wolff has demonstrated the increased vascularity of nervous tissue at synapses, presumably because here there is an important metabolic process going on: the conduction of an impulse from an axon to a dendrite by acetylcholine, a process requiring oxygen and furnished by the increased blood supply. Binz [26] said that the action of quinine as a cell toxin is due to interference with oxidation and showed that the changes produced in lower organisms by quinine are similar to those produced by lack of oxygen. Quinine probably interferes with oxidative processes at the synapse and the myoneural junction, depressing the action of acetylcholine.

Meyer and Gottlieb [27] cited Hoffman and Laqueur [28] in the statement that "the acid formation in blood from a vein is inhibited, and the formation of hippuric acid from benzoic acid and glycocoll [aminoacetic acid], when added to the blood perfused through the kidney, is decreased by quinine." The idea of inhibition of acid formation by quinine associates itself with the fact that acetylcholine is destroyed in an alkaline medium, being stable and preserved only in an acid medium.[29] Führer [30] too has demonstrated that acetylcholine is protected from esterase by increased hydrogen concentration; i. e., increased carbon dioxide tension. Perhaps the acidity (lactic?) of muscle in myasthenia is decreased as a result of some metabolic disturbance, thus neutralizing the expression of neural impulses, which finally depend on acetylcholine, ineffectual in too low an acid, neutral or alkaline medium. Conversely, the acidity of myotonic muscle may be such as to stabilize and implement the action of acetylcholine. Of course this idea is purely theoretical and only a guide to research. Speaking of congenital myotonia as far back as 1891, Jolly [31] speculated that the cause might be found rather in a disturbance in muscular chemistry than in the well known anatomic changes in muscle. His theory of half a century ago is more nearly fact today.

25. Wolff, H. G.: Site of Action of Acetylcholine and Its Significance, read before the Philadelphia Neurological Society, March 27, 1936.
26. Binz, C., quoted in an abstract of Wolfe, Eugene: Causation of Quinine Blindness, Lancet **1**: 1496-1497 (June 29) 1935, in Arch. Neurol. & Psychiat. 855 (Oct.) 1936.
27. Meyer and Gottlieb: Experimental Pharmacology as a Basis for Therapeutics, p. 501.
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SUMMARY AND CONCLUSIONS

Eighteen patients with myotonia atrophica and nine patients with myotonia congenita have been treated with quinine in the past year.

Quinine abolishes myotonus for as long as it is administered.

In two patients there was some diminution of myotonus after the administration of quinine was discontinued.

From 2½ to 5, 10 or 15 grains of quinine hydrochloride two or three times a day given by mouth has consistently eliminated myotonus as a disturbing symptom.

Nine patients with myasthenia gravis have been treated with prostigmine in the past year and a half.

Five patients have been restored to normal activity by 0.5 mg. of prostigmine given subcutaneously three or four times a day or one or two tablets (15 mg. per tablet) three times a day.

After early improvement four patients have become progressively worse as prostigmine medication was increased.

Increasing the dose of prostigmine appears to aggravate myasthenic weakness, probably by "curare-like" action.

Reduction of the dosage of prostigmine in these cases was followed by improvement.

Quinine and prostigmine have been assayed in the treatment of a good many other muscular disorders and found to be without benefit except in one case of facioscapulohumeral myopathy of Landouzy and Dejerine.

There is additional experimental evidence that myotonia and myasthenia are primary disorders of muscle or the myoneural junction.

410 East Fifty-Seventh Street.

ABSTRACT OF DISCUSSION

DR. PETER BASSOE, Chicago: The choice of me to open this discussion on muscular dystrophy is unfortunate, because not only have I little experience with the treatment of such cases but I confess to a certain lukewarm interest. I am tremendously interested in the prevention of muscular dystrophy. Physicians have been negligent because they know that muscular dystrophy really is a hereditary disease, and if they get the public to understand that it is a crime for people belonging to families with that disease to have children, this disease, as civilization progresses, will disappear from the earth. I know it is painful to do it. I remember how unhappy a young woman was who came to my office. Her father and her brother had dystrophy, and she herself had a stationary form, but I felt it was my duty to tell her—she wanted to get married—"It is all right for you to get married, but you should be sterilized first." With regard to myasthenia gravis, what little experience I have had with prostigmine has been extremely happy. Results have been most spectacular. Patients I have had under treat-

31. Jolly, F.: Ueber das elektrische Verhalten der Nerven und Muskel bei Thomsenscher Krankheit, Arch. f. Psychiat. **22**: S. 521, 1891.

ment for something like a year and a half have not had any ill effects. The dosage has been decreased and the effect more prolonged. When I began with these patients they were in bad condition. It was necessary to give them prostigmine by injection because they couldn't eat. I soon found that the result would carry over. For instance, a dose given at 5:30 in the evening enabled the patient to eat supper and also breakfast and then I changed, in those patients, to the prostigmine tablets, to be given by mouth. The results were satisfactory and I have an idea that perhaps the effect of the preparation taken by mouth is more prolonged. I have found prostigmine useful in cases difficult of diagnosis between myasthenia gravis and various other disorders. I found that the failure of any response to prostigmine settled the diagnosis in favor of something else rather than myasthenia gravis.

DR. B. LANDIS ELLIOTT, Kansas City, Mo.: This is a field in which there are many difficulties, both in diagnosis and in therapy. However, therapy has undergone rapid development recently. It might be said that in the case of myotonia and the muscular dystrophies there hasn't been any treatment worthy of the name until these recent communications. Until Dr. Wolf pointed out the value of quinine in myotonia there was nothing effective. A change has occurred in the emphasis on the line of attack in these diseases. There are many facts in the case of myasthenia gravis and myotonia particularly pointing to a possible endocrine origin. There is certain experimental evidence that endocrine disturbances affect the contractility of the muscle and in myxedema, for example, it has been pointed out that there is sometimes a hyperexcitability of muscle. There are a great many facts which cannot be harmonized by any theory or hypothesis yet put forward. At present the emphasis has shifted to the myoneural junction. It mustn't be forgotten, however, that the changes in muscle still demand explanation. The discovery of the action of quinine on myotonia is an important advance. It can be administered without much difficulty except for occasional idiosyncrasy, and there is some evidence that the effect may persist.

DR. H. E. HIMWICH, Albany, N. Y.: It has been suggested that the primary site of the lesion may be in the myoneural junction or in the muscle. It is possible that there may be a primary site in the myoneural junction and that the lesions in the muscle are secondary. In some preliminary work done in the laboratory in Albany the effect of quinine on the production of acetylcholine by brain slices has recently been studied. It was found that in the presence of minute amounts of quinine the production of acetylcholine was diminished. This seems to be suggestive, even though obtained on another tissue and not on the myoneural junction, that the therapeutic effect of quinine may be produced by diminishing the production of acetylcholine.

DR. KARL ROTHSCHILD, New Brunswick, N. J.: I had the same experience with prostigmine that Dr. Bassoe reports, the drug seeming to act better when taken by mouth. Patients take one, two or three tablets daily. I have found in a woman of 68 with myasthenia gravis, in itself an unusual case, that she has been doing well for about a year and a half with a decreasing amount of prostigmine by mouth. She reports that she does considerably better than with subcutaneous injections which I had originally given her. I should like to mention a case of amyotonia congenita in a child aged 6 months, who has done exceptionally well with a relatively large amount, almost the adult dose, of prostigmine.

DR. ALEXANDER WOLF, New York: Dr. Kennedy and I are aware that there are many endocrine changes in myasthenia gravis and in myotonia congenita. We know of cases of myotonia congenita with myxedema and have seen several cases of myasthenia gravis with exophthalmic goiter. We feel, however, that a great deal of responsibility for the symptoms lies at the motor end plate. It is interesting to hear that acetylcholine is diminished in the brain on the administration of quinine. We gave quinine after a spinal anesthesia and myotonus disappeared. In the light of this experiment it is our belief that quinine inhibits acetylcholine at the motor end plate or in muscle.

THE EFFECT OF DIURESIS BY MERCURIALS

ON THE CLINICAL COURSE OF CONGESTIVE HEART FAILURE

LAURENCE E. HINES, M.D.
CHICAGO

The course of congestive heart failure is so variable that statistical studies fail to complete a pattern which can guide the physician in determining the life expectancy of an individual patient. Dyspnea, usually the first sign of congestive failure, may exist for years before other signs develop. Some patients have rapidly increasing dyspnea, orthopnea and visceral stasis and die within a few weeks or months. The variability observed in these extremes and the intermediate variations can be explained by several factors, such as age of the patient, extensiveness of the etiologic agent, complicating pathologic conditions and faithfulness of the patient to the advice of his physician. Since statistics of mine or those of other observers can offer little aid in estimating the life span of patients with congestive failure, it is exceedingly difficult to determine the efficacy of a therapeutic agent for this condition. Opinions on the problem must for the most part rest on experience with thoroughly studied patients.

TABLE 1.—*Comparison of Flaxman's Series with Patients Treated by Mercurial Diuresis*

	Dead				Living			
	Flaxman's Series		Series Receiving Mercurials		Flaxman's Series		Series Receiving Mercurials	
Duration of Symptoms	Total	Per Cent	Total	Per Cent	Total	Per Cent	Total	Per Cent
1 day to 6 months....	136	75	28	58	329	78	*	
7 months to 1 year....	24	13	7	14	47	10	*	
1 to 5 years.....	18	10	12	26	48	11	12	100
Over 5 years.....	2	2	1	2	3	1	0	0

* All the living patients in this series were observed longer than one year.

TABLE 2.—*Incidence of Uremia*

	Total	Deaths from Uremia	Deaths from Uremia, Percentage
Flaxman's series.....	189	31	16
Series treated with mercurial diuretics	60	21	35

The treatment of the edema of congestive heart failure by mercurial diuretics has been practiced widely and with enthusiasm in recent years despite the fact that the removal of edematous fluid usually does not alter the progressive course of the underlying disease. Binger and Keith[1] commented on the complicated nature of the problem of edema and pointed out that there is no evidence to show that removal of edema has any curative effect on the primary disease. Nevertheless it is well known that edematous patients are symptomatically relieved by diuresis. It is also well known that rest in bed, digitalis and xanthine diuretics in some patients and at some time in the progress of the

From the Department of Medicine, Northwestern University Medical School.

Read before the Section on Pharmacology and Therapeutics at the Eighty-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1937.

1. Binger, M. W., and Keith, N. M.: The Effect of Diuretics in Different Types of Edema, J. A. M. A. **101**: 2009 (Dec. 25) 1933.

disease fail to act as diuretics. The literature [2] contains abundant evidence of the success of mercurial diuretics (salyrgan, mercuperin, merbaphen) in patients who did not respond to the simpler diuretic regimen. There are also numerous reports [3] of effective long-continued use of the drug with no harmful effects. A few reports deal with bad effects. Since merbaphen has been replaced, in general usage, by salyrgan and mercupurin, cases of mercurial nephritis are reported rarely.[4] As the mercury is completely eliminated from the body within twenty-four hours after administration,[5] an undesirable cumulative action is not feared. There are scattered reports of death after the use of diuresis produced by salyrgan. Immediate serious reactions with chill, rash and fever, ascribed to idiosyncrasy, have been reported by Cadbury [6] and Wolf.[7] The production of acute urinary retention in old men with large prostate glands has been attributed to the profuse diuresis produced by salyrgan.[8] Recently another type of harmful effect has been suggested by Poll and Stern.[9] They described a syndrome following mercurial diuresis which is characterized by preliminary symptoms of weakness, restlessness, mental confusion and psychosis, sometimes progressing to coma and death. Seven cases with three deaths were described. Because of poor turgor of the tissues, dry tongue, excessive thirst and recovery when salt and fluid were given, they attributed the syndrome to depletion of water and sodium chloride.

The present study was stimulated by the observation of occasional unfavorable reactions in some patients and an impression that the life expectancy of many patients was not prolonged even though edema was controlled. Further interest was stimulated by observation of patients who had uremic manifestations and died shortly after they had become edema free after prolonged mercurial diuresis. The following case report illustrates this feature:

C. S., a physician, aged 51, had had mild hypertension with slight albuminuria since 1918. No symptoms suggesting involvement of the heart or kidneys were present until bronchopneumonia developed in December 1935. Thereafter he noticed slight dyspnea on moderate exertion and occasional edema of the ankles. On April 15, 1936, the dyspnea was so severe that he was confined to bed, and progressive generalized edema ensued in the following two weeks. There was no significant diuretic response to the regimen of rest in bed, restriction of salt, digitalization and administration of xanthine diuretics. By July 5, 1936, the edema had caused a 20 pound (9 Kg.) increase in weight, the blood pressure was 186 systolic, 124 diastolic, albumin and casts were found in the urine, examination of the blood revealed 40 mg. of nonprotein nitrogen per hundred cubic centimeters and an electrocardiographic tracing revealed intraventricular block. Three days after the administration of ammonium chloride was started, 1 cc. of salyrgan was administered, and the dose was repeated at four day intervals from July 8 to October 2. A positive diuretic response (from 1,000 to 3,000 cc. net), usually lasting three days, occurred after each injection. During this period there was symptomatic improvement and a loss in weight of 40 pounds (18 Kg.) and the patient became edema free. One week before the last injection of salyrgan was given distaste for food, nausea, mental irritability and insomnia developed. The albuminuria had increased, and the nonprotein nitrogen content had risen to 70 mg. per hundred cubic centimeters. The mental irritability progressed to somnolence, stupor and coma, with death occurring Oct. 30, 1936, at which time a frost of uremic crystals was present on his face. At the time of death there was no edema of the lungs, subcutaneous tissue or serous cavities.

For a study of the duration of life of patients with congestive failure I selected a group of patients with hypertensive and arteriosclerotic heart disease from ward 25, Cook County Hospital, who were treated during 1935. The duration of life after the onset of congestive failure of the group treated with intravenous mercurial diuretics is compared with that of a group of patients from the same hospital studied and reported by Flaxman.[10] Table 1 gives the results of this comparative study. Minor differences in the lapse of time between onset of symptoms and death are too insignificant to allow the conclusion that mercurial diuretics alter the life span. Neither can any encouragement be derived from the fact that only twelve of sixty patients treated in 1935 are still alive.

TABLE 3.—*Uremic Symptoms*

Clinical Manifestations	Pathogenesis	Similar Changes in Mercurial Diuresis
Physical apathy, mental apathy, stupor, coma	Accumulation of aromatic phenol derivatives; chloride deficiency; magnesium excess (??)	Plasma chloride deficiency a common effect
Increase of neuromuscular irritability	Diminution of ionized calcium; accumulation of substances forming unionized calcium salts; excessive guanidine	Not observed
Tachypnea, cardiac asthma, acute pulmonary edema	Failure of the left side of the heart	
Slow deep breathing	Acidosis	Necessary for mercurial diuresis
Stertorous breathing and periodic breathing	Associated cerebral vascular changes; congestive heart failure; phosphate retention	Not observed
Lowered blood pressure	Effect of dehydration on phenols	Dehydration the desired effect
Vomiting	Bacterial action in gastrointestinal tract on secreted urea-producing ammonium salts	Increased concentration of blood urea
Anemia	Retention of phenols	
Purpuric manifestations	Calcium ion deficit	

The incidence of uremia in the patients who died is listed and compared with Flaxman's results in table 2. The incidence of uremia is more than doubled in the group which received mercurial diuretics. There is an obvious difficulty and hazard in drawing conclusions from this comparison because uremia is such an ill defined syndrome. Flaxman does not state the criteria for his diagnosis of uremia. A syndrome of mental and gastro-intestinal symptoms associated with nitrogenous retention and impaired function of the kidneys was the basis of diagnosis in my series. One cannot

2. Sprague, H. B., and Graybiel: Salyrgan as a Diuretic, Report of 60 Cases, New England J. Med. **204:** 154 (Jan. 22) 1931. Agnew, G. H.: Salyrgan as a Diuretic, Canad. M. A. J. **18:** 45 (Jan.) 1928. Bannick, E. G., and Keith, N. M.: Treatment of Nephritis and Nephrosis with Edema, J. A. M. A. **91:** 1944 (Dec. 22) 1928. Barker, M. H., and O'Hare, J. P.: Use of Salyrgan in Edema, J. A. M. A. **91:** 2060 (Dec. 29) 1928. Christian, H. A.: Types of Edema and Their Treatment, New England J. Med. **209:** 1267 (Dec. 21) 1933.

3. Dixson, I. M.: Salyrgan: Its Long Continued Use in Cardiac Failure, New England J. Med. **211:** 810 (April 12) 1934. Kramer, L. I.: Salyrgan: Its Use Over an Extended Period of Time to Relieve Cardiac Insufficiency, Rhode Island M. J. **17:** 175 (Oct.) 1934. Wiseman, J. R.: The Prolonged Use of Salyrgan as a Diuretic: Report of Two Hundred and Seventy Injections in Five Years in One Case, J. A. M. A. **99:** 114 (July 9) 1932.

4. Tarr, Leonard, and Jacobson, Sheldon: Toxicity of Mersalyl (Salyrgan): A Clinical and Anatomic Study, Arch. Int. Med. **50:** 158 (July) 1932.

5. Engel, K., and Epstein, T.: Die Quecksilberdiurese, Ergebn. d. inn. Med. u. Kinderh. **40:** 187, 1931.

6. Cadbury, W. W.: Idiosyncrasy to Salyrgan, M. Papers, Christian Birthday Vol., 1936, p. 259.

7. Wolf, I. J.: Idiosyncrasy to Salyrgan, J. A. M. A. **102:** 1177 (April 7) 1934.

8. Tscherning, Rüdiger: Ueber Salyrgan, Deutsche med. Wchnschr. **53:** 1465 (Aug. 26) 1927.

9. Poll, Daniel, and Stern, J. E.: Untoward Effects of Diuresis, Arch. Int. Med. **58:** 1087 (Dec.) 1936.

10. Flaxman, Nathan: The Course of Hypertensive Heart Disease, Ann. Int. Med. **10:** 748 (Dec.) 1936.

conclude from this small series that mercurial diuretics have the capacity per se to produce uremia. They do point to the necessity of a critical study of the arteriosclerotic patient with congestive failure before powerfully acting diuretics are used. Such patients as a class have general vascular disease and are likely candidates for uremia. In a recent review Harrison [11] emphasized the complicated nature of the problem of uremia. He stated that known and definite rôles in the pathogenesis of uremia can be ascribed as follows: Calcium ion deficiency as the result of the retention of products forming unionized calcium salts is concerned in the initiation of motor irritative phenomena; retention of phenol derivatives is related to the stuporous state; accumulation of organic and inorganic

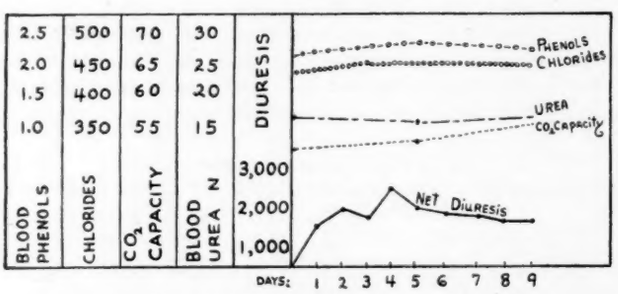

Chart 1.—Moderate diuresis in a 50 year old patient as result of rest in bed. There was no significant change in the blood phenol, the chloride or the urea nitrogen content or in the carbon dioxide combining capacity.

acids plus a loss of base have a rôle in the production of respiratory disturbance; depletion of chloride and water increases the catabolism of protein and at the same time further impairs the ability of the body to excrete the resulting metabolites. An examination of the reports on effects produced by mercurial diuretics reveals certain metabolic changes that are similar to those found in uremia. For example, increased excretion of water and chloride and decreased chloride content of the blood plasma are not only consistent features of mercurial diuresis but are associated with the uremic state. The production of acidosis, which according to Christian [12] and his co-workers is necessary for effective

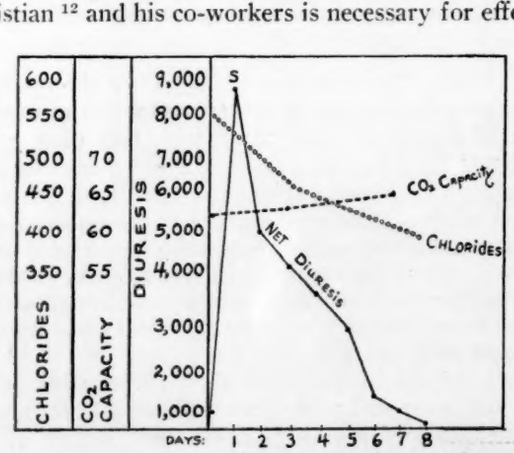

Chart 2.—Marked prolonged diuresis associated with moderate fall in the plasma chloride content but no marked change in the carbon dioxide combining capacity. *S*, salyrgan 2 cc.

mercurial diuresis, may also be prominent in uremia. An increase in the concentration of blood urea, well known as a part of the uremic picture, has been observed recently by Barker [13] after diuresis produced by salyrgan. Blumgart [14] has demonstrated increased excretion of sodium, potassium and calcium after mercurial diuresis, another possible factor in creating a metabolic disturbance. Table 3 contains a list of

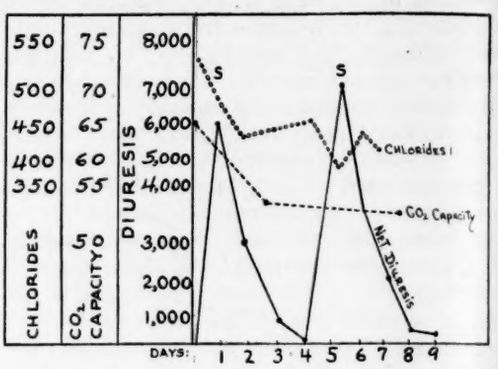

Chart 3.—Progressive lowering of the carbon dioxide combining capacity and the chloride content after repeated doses of salyrgan. *S*, salyrgan 2 cc.

uremic symptoms, their pathogenesis, according to the review by Harrison, and a comparable list of effects known to be produced in mercurial diuresis.

As a consequence of this study each patient with congestive failure is subjected to a more critical study before salyrgan is used. To prevent possible harm the following plan is instituted:

1. Salyrgan is used only when rest, digitalis and xanthine diuretics fail to produce the desired diuretic response.

2. The preliminary examination includes estimates of the plasma chloride content, the urea nitrogen con-

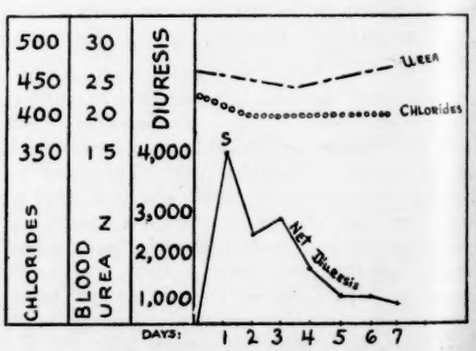

Chart 4.—No significant changes in the urea nitrogen or the chloride content after moderate diuresis. *S*, salyrgan 1 cc.

tent, the carbon dioxide combining capacity and the blood phenol content; the drug is not given if markedly abnormal values are observed.

3. During the period of diuresis interval determinations are made, frequently if symptoms suggest the onset of uremia.

4. Marked lowering of the plasma chloride content if associated with mental symptoms points to a need for intravenous administration of saline solution.

5. Lowering of the carbon dioxide combining capacity with symptoms of acidosis requires restriction of ammonium chloride and administration of sodium bicarbonate and dextrose.

6. The first dose of salyrgan should be given intramuscularly to eliminate the danger of the rare hypersensitive reaction.

11. Harrison, Tinsley R., and Mason, Morton F.: Pathogenesis of the Uremic Syndrome, Medicine **16**: 1 (Feb.) 1937.

12. Christian, Henry A.: Edema, Diuretics, Diuresis, Proc. Inst. Med. Chicago **11**: 149 (Nov. 15) 1936.

13. Barker, M. Herbert: Personal communication to the author.

14. Blumgart, Herman L.: Action of Diuretic Drugs, M. Papers, Christian Birthday Vol., 1936, p. 191.

7. Secretion of large amounts (from 5 to 10 liters daily) is more dangerous than secretion of smaller amounts; doses of from 0.25 to 0.5 cc. in some cases produce an adequate response.

Charts 1 to 5 present the results of examinations of the blood in five cases. There is no consistent picture either before or after mercurial diuresis. In some cases significant changes are brought about by the diuresis. Other evidence, previously quoted, substantiates the suspicion that marked diuresis is capable of instituting a metabolic upset which may have harmful effects on the patient. Further studies should be made to determine how such changes can be interpreted to the best advantage of the patient.

SUMMARY

A study of a series of hypertensive and arteriosclerotic patients with heart disease and congestive failure suggests a decrease in the duration of life after the use of mercurial diuretics. A high incidence of uremia was observed in the group. The known effects on the blood produced by mercurial diuretics show some points of similarity to the changes in the blood observed in uremia. Harmful effects from mercurial diuretics probably result from rapid removal of large quantities of edematous fluid rather than from mercurial damage to the kidneys. Mercurial diuretics should be used conservatively.

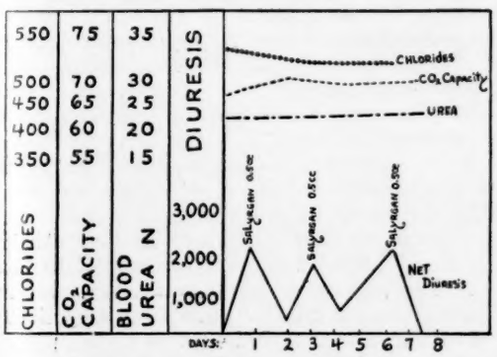

Chart 5.—Slight diuretic responses to small doses of salyrgan at frequent intervals: no significant changes in the phenol content, the carbon dioxide combining capacity, the chloride content or the urea nitrogen content.

104 South Michigan Avenue.

ABSTRACT OF DISCUSSION

DR. ARTHUR C. DEGRAFF, New York: Dr. Hines has rightly pointed out the difficulties that are encountered in determining the effect of mercurial diuretics on the life span of the patients. Any such study under controlled conditions at the present time would be impossible because I don't know of any one who is heartless enough to withhold mercurial diuretics from a patient who is markedly edematous and no longer responds to rest or digitalis. One has only to recall the fate of such patients in the premercurial diuretic era. Possibly one does not in any way lengthen the life and one may even, as Dr. Hines suggests, shorten the life of some of these patients. Even so I do not believe that mercurial diuretics should be withheld. However, the necessary precautions should be taken. Some of these Dr. Hines has already pointed out. It is fortunate that the mercurials of the present day have a fairly low toxicity. Even so one must be sure that the mercurial content is low. The lower the mercurial content, the less the possibility of kidney damage. There is the possibility that certain mercurial diuretics allow storage of mercury at the site of injection. Some work indicates that mercury is deposited at the site of injection and remains there for some time. The addition of theophylline to the mercurial diuretic will prevent such deposition of mercury at the site of injection. A mercurial combined with theophylline will allow the more rapid absorption of the mercurial diuretic and prevent local deposition of mercury. The proper preparation of the patient is necessary. These patients must be given adequate bed rest to see whether bed rest alone will remove the edema. They must also no longer respond to adequate doses of digitalis and they must have an adequate salt balance. Also it is important to combine the mercurial diuretic with ammonium chloride to get its full effect. Dr. Hines did not show in his cases how many had hypertension and what the results were before the mercurial diuretic was given. It is possible that a number of patients had severe kidney damage even before the mercurial diuretic was given. It is extremely difficult to make kidney function tests on patients who have marked edema. It would seem from my experience that the incidence of uremia in patients with congestive heart failure is not increased by the use of mercurial diuretics.

DR. JAMES G. CARR, Chicago: Dr. Hines has directed attention to a matter of clinical importance which heretofore has been generally neglected. The usual practice in the presence of marked edema occurring as a manifestation of congestive failure is to promote removal of the edematous fluid as promptly as possible. Dr. Hines has laid stress on two features of this plan of therapy, the failure of the rapid removal of edematous fluid to prolong the life for most patients and the danger to life that may ensue on the too hasty depletion of the tissues. Even though life is not prolonged by control of the edema, the symptomatic relief of passive congestion is fraught with so much comfort to the patient that from this standpoint alone the attempt to relieve or prevent edematous accumulation is indicated. But this indication must be qualified and the practice modified, if it appears that dehydration may be dangerous to the patient. Dr. Hines has made clear that a too rigid and rapid diuresis may be injurious, even fatal, particularly to those afflicted with hypertensive and arteriosclerotic disease. In a recent paper, M. Herbert Barker remarked, "We are too frequently tempted to watch the urine volume curve or weight drop without sufficient regard to the concentration of the waste products which may be less easily eliminated. Certainly, during diuresis, the piling up of minerals or medication with a resultant acidosis, uremic state or drug poisoning readily occurs." My interest in this subject was stimulated by a recent experience with an elderly patient at the Evanston Hospital. A woman of 74, known to have been under treatment for cardiac disease for at least two years, was admitted to the hospital for the second time within a few weeks. The average daily output of urine under urginin and ammonium nitrate during the first six days was a trifle under 500 cc. On the seventh day she was given 1 cc. of salyrgan, following which the twenty-four hour output rose to 1,380 cc. The patient's mental condition promptly became worse and she died on the third day thereafter. The blood chemistry was normal at the time of entrance. The exacerbation of her mental symptoms and the progressive failure of her general condition, appearing so abruptly after the use of the mercurial diuretic, with a marked increase of urinary output, were striking.

DR. CHAUNCEY C. MAHER, Chicago: We are much indebted to Dr. Hines for his accurate definition and timely warning of the possible unfavorable results with mercurial diuretics. In this group of patients with cardiac insufficiency and edema due to coronary thrombosis and myocardial infarction, a similar warning may be invoked. Too rapid elimination of edema fluid in the syphilitic type of heart disease and rheumatic valvular cases sometimes shows more temporary and less serious effects. On the other hand, one may disagree with certain of his suggestions of meeting this problem. One might question the rationale of subjecting all patients to "rest, digitalis and xanthine diuretics" before using the method of mercurial diuresis or the use of salyrgan. Secondly, his conclusions suggest the necessity of careful urologic study for obstructive uropathy and infection of the urinary tract. The type of patient that Dr. Hines has described not uncommonly has a urologic situation masked by the heart failure syndrome. The question may be raised as to the relationship of this type of extracardiac disturbance to the cardiac insufficiency.

DR. M. HERBERT BARKER, Chicago: This paper is of particular interest to me because in the cardiorenal vascular clinic

from 70 to 75 per cent of hypertensive vascular patients gradually acquire congestive heart failure. We have found it extremely important to dehydrate these patients slowly. The mild retention or moderate retention not only of urea but of other metabolites, particularly phosphorus and, as mentioned here, phenols and other toxic elements which become much more toxic as concentration is brought about by diuresis, makes it necessary that we do it slowly. I am sure that we have all seen one of the little brochures that show the wringing out of the sponge so quickly that we were quite impressed by this rather dramatic picture. However, a diuresis may be just about that dramatic, and it must be kept in mind that the kidney cannot always clear these waste products as fast as it does water. Sure enough, one may squeeze out the water but not so with the retained metabolites. According to my experience the result has been that one drives urea up, which may not in itself be especially toxic, but associated with it there is the concentration of these other waste products, particularly phosphorus, with a resultant severe acidosis and further progression of a uremic state and the patient slips rapidly into a state of coma. Caution, as Dr. Hines emphasizes, needs to be emphasized from time to time.

DR. LAURENCE E. HINES, Chicago: I am grateful for the discussion. I hope I did not give the impression that mercurial diuretics are harmful to all patients. This presentation is chiefly a plea for the use of drugs capable of producing minor diuresis in preference to those which produce marked diuresis. In connection with Dr. Maher's remark about the early use of salyrgan, I do not believe it should be used if minor diuresis can be effected by a simpler regimen. Dr. DeGraff asked about the incidence of hypertension. About half of the patients at the time we saw them had hypertension.

Clinical Notes, Suggestions and New Instruments

THE EFFECTS OF TOXIC DOSES OF BENZYL METHYL CARBINAMINE (BENZEDRINE) IN MAN

SYDNEY P. WAUD, M.D., CHICAGO

Benzedrine is a synthetic drug which is in common use today and frequently is taken without medical supervision. The benzedrine inhaler has been used extensively in infections of the upper respiratory tract; benzedrine solution has been used locally less frequently in this condition. Benzedrine sulfate has been used internally with success in the treatment of narcolepsy and in cases of orthostatic hypotension. It is interesting to note that in my experiments toxic doses of benzedrine sulfate produce orthostatic hypotension constantly for several hours after the original stimulation of the sympathetic nervous system has subsided.

In the experimental study of the effects of toxic doses of benzyl methyl carbinamine by inhalation, it is a most difficult task to determine the amount of the drug absorbed and its manner of destruction and elimination in the human body. It is important to note that the toxic doses used in the experiments given here have no counterpart in clinical use. However, with therapeutic doses the majority of reported untoward symptoms compare closely with the constant symptoms noted with toxic doses of benzedrine. The subject used in these experiments was a normal man, aged 27, weighing 97 Kg. Eight separate experiments were carried out in all, each being from seven to ten days apart. In each experiment two new benzedrine inhalers were used simultaneously and were inhaled normally and at times deeply for periods of from four to six hours continuously. Exhalation was always done through the oral cavity. Each inhaler is reputed to contain from 0.305 to 0.360 Gm. per tube, 0.325 Gm. being accredited average. Benzedrine, being volatile, was negligible in the tubes at the conclusion of each experiment. It was calculated that approximately 650 mg. (10 grains) was inhaled in each experiment (6.7 mg. per kilogram of body weight). It is, of course, unlikely that all of the drug inhaled was absorbed. The estimated absorbed doses was believed to be approximately 400 to 500 mg. This was checked in one experiment by ingestion. This would be approximately fifty times the usual therapeutic dosage of benzedrine sulfate by mouth; it is approximately 1,000 times the usual therapeutic dosage of the inhaler—two inhalations an hour. The menthol in the inhalers is not absorbed, but it does produce a local pseudo-anesthesia of the nares. The oil of lavender is not absorbed and produces no known local effects. All symptoms and signs recorded were constant in all experiments unless otherwise stated.

It is known that therapeutic doses of both ephedrine and benzedrine produce different results both quantitatively and qualitatively in different individuals. However, ephedrine in toxic doses usually produces different quantitative changes in different individuals. This would appear to be true of benzedrine in toxic doses also. It would, of course, be advisable to have more data from several other cases to assure the present results; however, the experiments are quite harsh for voluntary help, and it would be absolutely unwise to use unknowing patients.

The absorption of large quantities of benzedrine (approximately 650 mg.) by inhalation in one experiment caused a questionable paralysis of the sympathetic system, and the heart was controlled by the vagus system. This was a clinical observation. In my eight experiments the rise of blood pressure with the inhalation of benzedrine was constant and did not return to normal for ninety-six hours. However, at no time was albuminuria present. With toxic doses of benzedrine the great loss of appetite with resulting rapid loss of weight was due to the marked relaxation of the entire gastro-intestinal tract. The water content of the body was greatly reduced. An increased metabolism was suspected but was not checked by laboratory methods. The physical activity, of necessity, was minimal. After the effects of the drug had disappeared, the weight quickly returned to normal even though from 10 to 14 pounds (4.5 to 6.4 Kg.) had been lost on an average during the three to four day period following inhalation. With toxic doses of benzedrine the stimulation of the central nervous system remained for several hours after cessation of inhalation, but following this a marked mental depression and general fatigue was constantly present for from three to four days.

A definite tolerance of the body for benzedrine is slowly built up, and increasing doses are necessary to produce the original effects. The question of addiction to benzedrine is not settled, but I believe the possibility is not to be treated lightly, for most drugs that produce a pleasant effect on the brain (either stimulating or quieting in nature) have their addicts.

Toxic Signs and Symptoms Due to the Inhalation of Benzedrine

Eyes:
1. Slight blurring on near vision.
2. Dilatation of pupils with peculiar glaring appearance, which remains for 6 to 12 hours after cessation of inhalation.
3. Reaction to light and in accommodation sluggish.
4. Slight conjunctival injection.

Nose:
1. Loss of smell (immediate).
2. Pseudo-anesthesia of nasal passages (menthol).
3. Numbness and coldness of nose.
4. Extreme dryness of nose, especially the post nares, which lasts for 36 to 48 hours.
5. Moderate amount of mucous secretion which starts about 12 hours after inhalation and lasts from 2 to 4 days.
6. Occasional petechial hemorrhagic areas in nares.

Ears:
1. Slight tinnitus toward end of inhalation.
2. Moderate pounding in ears at end of inhalation.

Mouth:
1. Marked dryness for 24 hours.
2. Marked salivation in experiment 8 only.

Pharynx:
1. Marked dryness for 24 hours.
2. Extreme soreness of throat (three occasions), which lasted for 48 hours and was temporarily relieved by sodium bicarbonate gargle.
3. Moderate redness of pharynx.
4. Postnasal drip present for 24 hours.

Lungs:
1. Marked emphysema for 24 hours.
2. Many moist rales for 24 hours which clear with coughing.
3. Whitish foamy sputum for 24 hours.
4. Moderate dyspnea on exertion (72 hours).
5. Cyanosis absent.

Review of the literature has been omitted from THE JOURNAL but will appear in the reprints.

Heart:
1. Unable to percuss borders for 6 to 8 hours after inhalation.
2. Heart beat forceful but barely palpable.
3. Many extrasystoles for 4 to 5 days.
4. Paroxysmal tachycardia on two occasions after cessation of inhalation.
5. Murmurs absent.
6. Rhythm of heart unstable and sinus arrhythmia present.
7. Slight exertion producing marked tachycardia. Moderate tachycardia at rest for two days.
8. Aortic second tone markedly accentuated, and ringing was noticed on two occasions.
9. Pulmonary second tone moderately accentuated for few hours.
10. Bradycardia on one occasion at end of inhalation (vagus rhythm).
11. Rate 96 to 120 during inhalation, 80 to 90 for 4 to 5 days at rest (normal 72 to 76).
12. Orthostatic hypotension for 24 hours after cessation of stimulation.

Gastro-Intestinal:
1. Extreme loss of appetite for 48 to 60 hours.
2. Appetite extreme after 4 days.
3. Loss of weight 10 to 14 pounds, which was regained in a week.
4. Belching moderate for 2 days.
5. Flatulence extreme for 60 hours.
6. Abdominal distention marked for 48 hours.
7. Slight general abdominal discomfort in 2 to 3 hours after cessation of inhalation.
8. Occasional pain referred to precordium and disappeared with passage of flatus.
9. Constipation 4 to 5 days.
10. Diarrhea without colic (one occasion).
11. On two occasions typical pyloric spasms present which were relieved in 15 to 20 seconds by alkali. Occurred 48 hours after cessation of inhalation.
12. Peristalsis decreased for 24 hours.
13. No nausea or vomiting.

Genito-Urinary:
1. Marked shrinkage of mucous membrane of external urethra.
2. Immediate diuresis (2,000 cc. on one occasion. Usually 500 to 1,000 cc.) in 4 to 6 hours.
3. Moderate suppression of urine after 8 hours for 24 hours.
4. Decreased control of sphincter urethrae both in starting and stopping stream.
5. Call to urination not present till marked bladder distention.
6. Markedly decreased force of stream.
7. Thirst absent in all experiments.

Skin:
1. Marked coldness of extremities for 24 hours.
2. Blanching of extremities with marked flushing of face and neck for 24 to 48 hours.
3. Small erythematous patches around neck and shoulders.
4. Marked tingling of skin, especially in extremities, during test and for several hours following.
5. Slight decrease in sensation of extremities for several hours.
6. Transitory chilly sensations in different areas of body for 24 to 48 hours.
7. Generalized flushing of skin after 12 hours for 12 to 24 hours.
8. Perspiration diffuse during inhalation. Peculiar odor present. On occasion perspiration continued for 4 to 6 hours after cessation of inhalation.

Vessels:
1. Marked visible and palpable pulsations of all superficial arteries (including radial at wrist and dorsal pedis).
2. Bounding pulse at rest.
3. Weak and thready pulse with exertion.
4. Increase of size of superficial veins.

Brain:
1. Numbness of brain at end of inhalation.
2. Attacks of cerebral anemia on assuming erect position for 24 hours. (Cause: splanchnic dilatation with inefficient cardiac response.)
3. Increased mental activity during inhalation with decrease in mental efficiency.
4. Decrease in memory for 2 to 3 days.
5. Moderate euphoria during inhalation.
6. Marked insomnia for 48 to 72 hours.
7. Secondary mental depression for several days.
8. Moderate general weakness and fatigue for several days.
9. Increased libido during and for short period following inhalation.
10. Decreased libido from two hours to four days following inhalation.

Extremities:
1. Coarse tremor of hands for 24 hours.
2. On several occasions blanched areas accompanied by moderate pain were present. Heat gave relief.
3. Pains in the muscles of the lower extremities 4 to 6 hours after inhalation on two occasions (experiments 7 and 8).
4. Toxic papular erythema on extremities for 36 hours (experiment 8).
5. Mottling of the skin especially noticeable in the hands for 24 to 36 hours.
6. Moderately increased reflexes for 24 hours.

Laboratory Examinations

Urine:
Specific gravity 1.002 to 1.005 first specimen.
1.008 to 1.012 second specimen.
1.018 to 1.036 third specimen.
Albumin not present in any specimens.
Sugar not present in any specimens.
Casts not present in any specimens.
Red blood cells not present.
Few white blood cells occasionally.

Stool:
No pathologic changes except extreme costivity.

Electrocardiogram:
Normal before and after inhalations.
Slight sinus tachycardia 2 days after last inhalation.

Blood Pressure (Average):
Before inhalation 118/80.
At end of inhalation 175/102.
After two days 145/95.
After four days 120/84.

CONCLUSIONS

1. Continuous inhalation of benzedrine can produce definite toxic effects characteristic of sympathomimetic excitation, stimulation of the central nervous system and depression of the cardiac muscle.

2. Ephedrine and benzedrine are pharmacologically very similar in toxic doses.

3. Benzedrine in toxic doses reduces libido moderately after sympathetic stimulation subsides.

4. The pressor effect of benzedrine is marked but relatively temporary.

5. Benzedrine in toxic doses is a diuretic in normal individuals.

6. The stimulation of the central nervous system is marked but relatively temporary and is always followed by marked fatigue and mental depression when toxic doses of benzedrine are absorbed.

7. Permanent organic changes are probably negligible with normal doses of benzedrine over long periods of time.

8. The margin of safety of benzedrine is great in normal persons.

9. The likelihood of addiction is quite possible.

10. The indiscriminate use of benzedrine is very unwise.

30 North Michigan Avenue.

CANCER, DESICCATION AND CHEMISTRY

EDWARD G. MARTIN, M.D., DETROIT
Attending Proctologist, Detroit Receiving Hospital

Heat used in the treatment of cancer was never satisfactorily effective until the introduction of the modern diathermy machine. There is now available for desiccation purposes 3,500 (F.) degrees of controlled heat. It is of historical interest to note that Hippocrates used hot irons in the treatment of cancer of the breast 2,000 years ago; Percy's work with the cautery is of contributory value; so was Crookall's [1] work with diathermy, reported in 1926. Strauss and his associates [2] appear to have taken the use of "surgical diathermy" more seriously and report several years of favorable and interesting experience.

FIRST CLINICAL THREE YEAR CURE

In June 1935 I [3] reported (case 1) my first clinical cure of advanced cancer of the rectum; this patient had a liver metastasis. His major treatment by fulguration or desiccation was in May 1934; the second and last (minor) fulguration was in October 1934. After three years he still remains clinically free from any symptoms of cancer. Case 1 was reported as clinical evidence in support of my supposition that cancer is a slow individual reaction to an unidentified substance [4]—an allergy. I now add four consecutive cases of well advanced adenocarcinoma of the rectum that have been treated by radical desiccation. All five patients have been free from evidence or clinical symptoms of cancer from one to more than two years. The diagnosis in all five cases was clinically well advanced carcinoma, proved by expert microscopic study. These comprise all the private cases that were treated by radical desiccation, and all would be considered operable by most standards except case 1. My experience in clinic cases at Receiving Hospital, where cancer in the most advanced degree comprised most of them, was illuminating and the improvement observed was sufficiently encouraging to warrant the experimental trial in private cases of less advanced degree. Let me declare that I now have no hesitancy in desiccating a so-called operable carcinoma situated entirely within the rectum and that I do so with an increasing confidence of producing a "clinical recovery." By "clinical recovery" I mean just what that statement implies;

Read before the American Proctologic Society, Atlantic City, N. J., June 8, 1937.

1. Crookall, A. C.: Treatment of Cancer of Rectum by Percy Cautery and Endothermy, Tr. Am. Proct. Soc., 1925, Northwest Med. **25**:258 (May) 1926.

2. Strauss, A. A.; Strauss, S. F.; Crawford, R. A., and Strauss, H. A.: Surgical Diathermy of Carcinoma of the Rectum, J. A. M. A. **104**:1480 (April 27) 1935.

3. Martin, E. G.: A Hypothesis as to the Etiology of Cancer, Tr. Am. Proct. Soc., 1935.

4. Abrikosov, A. I.: Morphologic Manifestations of Allergic Reactions in Man, Sovet. khir. **10**: 619, 1933.

the entire disappearance of the growth with regeneration of mucous membrane: disappearance of cachexia, gain in weight, and such general recovery in health the loss of which may have resulted from the malignant growth. Scar tissue, which may be a complication, has not occurred in any of these five cases.

Various conclusions will necessarily be drawn when a number of men apply different technics to widely divergent degrees of involvement. It must be realized that the majority of those using some form of heat application do not expect recovery, and those who have been courageous enough to mention it at all suggest it for palliation only in advanced cases. In spite of my optimism, I am constrained to assert that desiccation is still experimental. More experience will develop a technical standard for the application of electrodesiccation; then a composite experience will be of greater value.

THE TECHNIC AND ITS DANGERS

Desiccation is a dangerous procedure requiring expert surgical and anatomic knowledge. One must have adequate exposure, preferably in the knee shoulder position with 50 mg. of spinal anesthesia. Insulated equipment is desirable, as well as a sucker to remove the smoke. A high tension ark using the machine's capacity with a spark devoid of the flame developed in a number of the tube machines is important. A part of the procedure consists of cooking the tissue by deep insertion of an electrode, as well as fulgurating and desiccating it from the surface. "Cauterization" has no place in this procedure. (I am not describing palliative treatment.) Hemorrhage can be profuse and fatal; a perforated bowel and death may result when fulguration is done above the peritoneal reflection. It is a major radical surgical procedure to be used skilfully and with courage, if satisfactory results are to be anticipated. It is my intention to desiccate the entire growth whenever possible and to finish with a second and often final treatment in approximately two weeks. Examination should be made monthly and further desiccation administered as indicated by observation. Biopsies should be used to differentiate granulation tissue from cancer growth.

So much as has been related I believe can be substantiated in fact and in principle by the experience of a number of other investigators.

Such results as have been seen simply must arouse interest and speculation, even among the conservative. Local excision of malignant growths has been considered bad surgery for years; it has long been discarded because experience disclosed a prompt recurrence either locally or by metastasis in the great majority of cases. Modern surgical technic comprises the most radical procedure commensurate with reasonable safety because of the lymphatic spread—"everything to gain and very little to loose."

Desiccation seems to offer some hope of the development of a better method in treating cancer; when I stress a "better method" I do not refer to the desiccation treatment; actually its field of application is very limited. Something has to account for the remarkable results that have accrued by burning cancer tissue; it is not reasonable or intelligent to dismiss what one has seen with a "wise crack" and assume a defeatist attitude that "cancer can't be cured."

It is common knowledge, at least among biochemists, that much chemistry is evolved when tissue is burned. It seems to me that among the chemicals resulting from desiccation and fulguration of cancer is one or a combination of several that influences metastasis. It is known that heat of a reasonably mild degree destroys cancer cells, which can account for a local disappearance. The intense heat that I have used penetrates deeply, more deeply I believe than radium, yet that does not account for an effect on the more distant metastases. It could be and may be a chemical action or desensitization, and if so it can and will be proved by its recovery in solution. Its recovery affords the possibility, if not the probability, of identification. Further possibilities then become unlimited.

I have made a filtrate from desiccated cancer tissue but have progressed as yet to no reportable conclusion. There is no reason to believe that the chemistry must result from fulgurated cancer tissue; any tissue, such as placenta, should do.

The question has been properly asked, If chemistry is a recovery factor why do not advanced cases exhibit more uniform improvement? If chemicals are a determining factor, an insufficient quantity is developed by the limited desiccation to overwhelm extensive involvement. The question as to why cancer of the bladder does not respond more uniformly to fulguration may be answered by the fact that fulguration is limited by the fear of puncture and therefore very little chemical reaction could be expected.

I have the greatest admiration for the remarkable progress made in modern surgical procedures dealing with cancer; however, I shall have a much greater admiration for any method that will cure cancer without surgery. It may be possible—who knows?

1447 David Whitney Building.

ENCEPHALOPATHY FROM THE THERAPEUTIC USE OF LEAD AND OPIUM PILLS

WILLIAM R. GERAGHTY, M.D., BALTIMORE

Because of the small dose and short period of administration, it is unusual to have toxicity from an ingested medicinal soluble lead salt. Rarely has the intoxication been of the encephalic type. Nevertheless a small dose, long continued, may produce encephalopathy, as is shown in the following report.

REPORT OF CASE

History.—G. G., a man, aged 43, admitted to the neurosurgical service of St. Joseph's Hospital Jan. 25, 1937, complained of headache, mental confusion, muscular weakness and epileptiform convulsions. The family history was unessential. He had active pulmonary tuberculosis, complicated by intestinal tuberculosis, necessitating the removal of 12 inches (30 cm.) of terminal ileum, the cecum and ascending colon on June 10, 1936. After this diarrhea developed, for which, beginning August 29, he took a pill containing 1 grain (0.065 Gm.) each of lead acetate and opium, twice a day. Except for one seven day period, this was continued until Jan. 19, 1937. The onset of the present illness was indefinite. Tremor of the right side of the face, pallor of the skin, muscular weakness and loss of weight were noticed about December 25. After a temporary loss of consciousness, Jan. 17, 1937, memory was grossly impaired and he was clouded, confused and disoriented. Amblyopia and continuous right frontal headache both became troublesome. January 24, after two generalized convulsions, he was delirious and had to be restrained.

Examination.—The temperature, pulse and respiration were normal and remained so throughout. Blood pressure was 120 systolic, 60 diastolic. He was obfuscated, irrational and resentful of examination. There was marked pallor of the skin and mucous membranes and a lead line on the gingiva of four carious lower incisor teeth. Both optic disks were pale and the retinal veins full. An old choroidoretinitis with exudate was present on the right. The left upper and lower cutaneous abdominal reflexes were absent. All deep tendon reflexes were exaggerated. A fine tremor was present in both arms. The left leg was weak and both feet and ankles were edematous.

Examination of the blood revealed: red cells 2,550,000, hemoglobin 46 per cent, white cells 15,750, polymorphonuclears 80 per cent, lymphocytes 16 per cent, mononuclears 2 per cent, eosinophils 2 per cent. Stipple cells averaged 26,000 per million red cells. Anisocytosis, with macrocytes predominating, and poikilocytosis were present. The blood was of group 4. The Wassermann reaction was negative. Blood chemistry revealed nonprotein nitrogen 0.35 mg. per hundred cubic centimeters, and sugar 0.7 mg. January 27 the lead content was 0.37 mg. per hundred grams of blood.[1] The spinal fluid, under a pressure of 16 mm. of mercury, was clear and contained 4 mononuclear cells per cubic millimeter and a trace of globulin. The Wassermann reaction was negative. The lead content was 0.042 mg. per hundred grams of fluid. Urinalysis revealed an acid reaction, specific gravity of 1.014 and no albumin or sugar. The lead content was 0.39 mg. per liter of urine.

Roentgenograms showed faint lead deposits in the upper epiphysis of the radius, ulna and tibia.

1. The Baltimore City Health Department made the examinations for lead, using the diphenylthiocarbazone (Dithizone) technic.

Therapy.—Fifteen grains (1 Gm.) of calcium chloride intravenously twice a day and 15 grains (1 Gm.) of calcium gluconate by mouth, three times a day, was continued until March 28. In addition he was given iron and ammonium citrate, 30 grains (2 Gm.) three times a day. Parenteral liver therapy for two weeks made no appreciable increase in the red blood cells.

Course.—Convulsive seizures, from one to four each day, persisted until January 29; however, he was irrational and required restraint until February 3. He frequently vomited dark bile stained fluid, was incontinent and often refused medication. Headache continued throughout February. February 22 the stipple cell count was 19,000 per million red cells. March 3 the feces contained 0.23 mg. of lead per hundred grams and 0.12 mg. per gram of fecal ash. March 15 the saliva contained 0.015 mg. of lead per hundred grams. March 25 the blood examination showed red cells 3,560,000, hemoglobin 82 per cent, white cells 9,250, polymorphonuclears 60 per cent, lymphocytes 24 per cent, mononuclears 12 per cent, myelocytes 4 per cent. Anisocytosis and poikilocytosis were less marked. The lead content of the blood was 0.15 mg. per hundred grams. Blood calcium was 9.9 mg. per hundred cubic centimeters of serum. Three-tenths cubic centimeter of sweat contained 0.0004 Gm. of lead. March 29 the spinal fluid, under a pressure of 8 mm. of mercury, contained 2 mononuclear cells per cubic millimeter and was globulin free.

Diarrhea, from five to eight stools a day, did not retard improvement, and a gain of 16 pounds (7.3 Kg.) was made by April 1.

The patient was discharged April 3 without evident mental aberration and free from tremor but with slight general muscular weakness.

In the follow-up record April 22 the blood examination revealed red cells 4,950,000, hemoglobin 80 per cent, white cells 10,650, polymorphonuclears 87 per cent, lymphocytes 12 per cent, mononuclears 1 per cent. There was a moderate degree of anisocytosis and poikilocytosis. Stipple cells averaged 1,000 per million red cells. The reticulocyte count was 2.95 per cent. Blood calcium was 12.8 mg. per hundred cubic centimeters of serum. The lead was 0.11 mg. per hundred grams of blood. The neurologic signs were essentially negative. At the time he had a headache. The changes in the right fundus were unaltered. The lead line was less prominent. June 25 the lead was 0.092 mg. per hundred grams of blood.

COMMENT

The general health of this patient was previously depleted by advanced tuberculosis, which it is believed predisposed to the plumbism. He was admitted with the provisional diagnosis of tuberculoma of the brain; it was two days later that lead encephalopathy was determined. The total ingestion of lead acetate was 274 grains (17.75 Gm.) in less than five months. There is no parallel between this amount and that actually absorbed from the alimentary canal. Nor is it possible to fix a time when toxicosis really began—before the lead content of the body fluids reached the high level present on admission.

A previous resection excluded the terminal ileum and part of the colon from participation in either the absorption or the elimination of the lead.

It is to be remarked that the spinal fluid did not show a pleocytosis, but the pressure of 16 mm. of mercury on admission must be considered high when compared with an 8 mm. pressure two months later.

In the lead fixation therapy there were no manifest deleterious effects from the intravenous use of the calcium chloride. Lead in the blood stream was reduced approximately 33 per cent in four weeks and 60 per cent in two months. In the lead estimations the whole blood was used for testing.

Obviously it is important that no effort be made to delead this man and every effort be made to reduce the lead in the circulating blood stream by maintaining a positive calcium balance.

CONCLUSION

Ingested lead acetate, in small doses over a long period, can produce encephalopathy.

10 East Biddle Street.

Council on Pharmacy and Chemistry

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

CREOSOTE AND GUAIACOL COMPOUNDS OMITTED FROM N. N. R.

For some years the Council has considered the lack of evidence for the usefulness of creosote and guaiacol preparations administered orally for their supposed action on the respiratory passages. The products Calcreose (Maltbie Chemical Co.), Creosotal-Winthrop, Benzosol, Duotal (Winthrop Chemical Co.), Proposote (Parke, Davis & Co.) and Thiocol-Roche, fall into this classification; three of them—Calcreose, Duotal and Thiocol-Roche—were included in the first edition of New and Nonofficial Remedies in 1907 and the others were accepted at various times up to 1925. Guaiacol Sulphonate-Merck, included in the accepted but not described section of N. N. R., also comes under this consideration. The acceptance of these products was based mainly on the ground that the claims for their efficacy were in harmony with generally accepted opinion and their acceptance was continued because they were reconsidered mainly with reference to claims previously made and not at the time questioned by most pharmacologists and clinicians.

I. PHARMACOLOGIC STATUS

The present views of the leading pharmacologists are expressed in closely similar terms in the textbooks of Cushny, Meyer and Gottlieb, and Sollmann. The latter states:

"Uses.—Creosote and guaiacol were extensively employed in tuberculosis, having been introduced especially by Sommerbrodt, in 1887; but they have gone out of fashion since the clinical benefits did not prove sufficiently definite, and the laboratory results were quite negative."

With reference to other claimed effects—promoting appetite and digestion, lessening cough, and so on—Sollmann (A Manual of Pharmacology, ed. 5, p. 617) states:

"It would be still more difficult to explain the effects. The tubercle bacilli are certainly not killed in their foci; it is doubtful whether their growth is restrained." . . . "Thiocol is potassium guaiacosulphonate, analogous to sodium phenolsulphonate. Like the latter, it has very little effect."

II. CURRENT LITERATURE

The Council has given consideration to the current literature, which affords no satisfactory evidence for the usefulness of these preparations. In this connection it is interesting to note that Clark and Kirch (*J. Am. Pharm. A.* **24**:564 [July] 1935) state that "Search of the available literature reveals no records of painstaking pharmacological work on this substance [potassium guaiacol sulfonate]."

Other articles were considered by the Council but only one of them seems to suggest that these compounds are of definite therapeutic value in the conditions for which they are commonly used. It is difficult to evaluate the part played by guaiacol carbonate in the results reported by R. Burnand (Guérison clinique contrôlée après six annés d'une tuberculose intestinale ulcéreuse inopérable, *Bull. et mém. Soc. méd. d. hôp. de Paris* **54**:875 [May 26] 1930), since he used various other measures in addition to the guaiacol compounds.

Consideration was also given to three manuscripts submitted by Professor Livingston of Temple University. These consisted of studies conducted by Edwin J. Fellows, under a grant from Maltbie Chemical Company, manufacturer of Calcreose; they were: I. Calcium Creosotate: Chemistry; II. Calcium Creosotate: Bacteriology; III. Calcium Creosotate: Elimination. It is the opinion of the Council that not one of these studies affords evidence of the therapeutic value of Calcreose. These papers have been published in the *Journal of Pharmacology and Experimental Therapeutics* **57**:122 (June) 1936; **60**:178, 183 (June) 1937, under the title "Studies on Calcium Creosotate."

Among other articles cited by Hoffmann La-Roche, Inc., manufacturer of Thiocol-Roche, was the thesis of Pierre Febvre. A letter was addressed to the Laboratories of Chemistry and Physiology of the School of Medicine and Pharmacy of Clermont, France, requesting a copy and the Council, after giving it due consideration, came to the conclusion that it contained nothing that bears directly on the rationale for the clinical use of the Hoffmann La-Roche product.

After reviewing the cited references, as well as others, including those submitted by the manufacturers, the Council decided that they afford no satisfactory evidence that these products have any important effect. It is indeed strange that drugs which are used as extensively as claimed by the manufacturers would have so little back of them in the literature; this is especially true of products that are far from new.

III. CLINICAL EFFICACY

The Council, anxious to give thorough consideration to all phases of the matter, decided to obtain the opinions of certain members of the medical profession as to the efficacy of these products.

The following information was derived entirely from the replies to inquiries sent to the active membership of the Association of American Physicians and the American Pediatric Society (see end of report). To the 286 inquiries made, 180 replies were received; however, fourteen of the physicians who replied were not in practice and hence had no occasion to prescribe these remedies. Of exceeding interest was the fact that only three of the remaining 166 stated that they used the preparations frequently, while 108 have not used them at all in recent years. The remaining fifty-five use them occasionally or rarely. That some physicians would still be using one or more of them is not su prising in view of the fact that these preparations have been used to some extent in the past and are being constantly advertised to the medical profession. It must be remembered in considering these figures that these drugs are recommended in conditions that would call for frequent use if they were considered to be of unquestioned benefit, since there are so many patients in the class for which these substances are said to be employed.

Further consideration of these replies indicates that not one of the 166 members had any knowledge of a "blind test" of these substances and that most of them merely reported their impressions. Furthermore, many of those who occasionally use these substances expressed some doubt of their being worth retaining, or at least made no attempt to justify their inclusion in N. N. R. This is taken as an indication that these agents were used for the most part empirically. Only three or four of the members of these two organizations made any sort of vigorous defense of the preparations and these were based on clinical impressions rather than on exact knowledge of their mode of action.

IV. OTHER CONSIDERATIONS

While the Council had this matter under advisement, the A. M. A. Chemical Laboratory undertook to evaluate better standards for New and Nonofficial Remedies for potassium guaiacol sulfonate. The Heyden Chemical Company wished to submit its product Potassium Guaiacol Sulphonate but as a result of preliminary discussion with the A. M. A. Chemical Laboratory on the matter of standards, the product was never formally presented to the Council. The Laboratory could not confirm either the revised tests and standards submitted by Heyden Chemical Corporation or those of Hoffmann La-Roche, Inc. Notice to this effect was sent to the two firms. Hoffmann La-Roche, Inc., replied that it would take up the matter with its principals in Switzerland; no further reply has been received from this firm. The Heyden Chemical Corporation in reply to a follow-up letter called attention to the fact that the National Formulary had published a galley proof of a proposed monograph and that its product met National Formulary requirements. In reply the A. M. A. Chemical Laboratory pointed out that the assay method given in the proposed National Formulary monograph was not workable.

In view of the foregoing considerations the Council voted that all manufacturers of accepted creosote and guaiacol preparations be informed that after the expiration of the longest period for which any one of them stood accepted (one year from date), no compound of this type would be reaccepted or accepted for N. N. R. without convincing evidence of the therapeutic value claimed. The Council's secretary forwarded this decision to all firms whose products of this class are now in N. N. R.—the Maltbie Chemical Company, the Winthrop Chemical Company, Inc., Parke, Davis & Company, and Hoffmann La-Roche, Inc.—with the suggestion that in the meantime they might care to submit further evidence for the therapeutic value of these products.

The Maltbie Chemical Company replied that it had established a three year fellowship, which resulted in the three articles by Fellows already mentioned. A second reply from Maltbie Chemical Company noted that it had initiated studies to demonstrate the therapeutic usefulness of Calcreose.

The Winthrop Chemical Company presented no evidence bearing on the question at issue.

Parke, Davis & Company stated that it believed the compounds were useful but that it was not promoting any products of this description and hence was not interested in undertaking the accumulation of clinical evidence.

Hoffmann La-Roche, Inc., replied submitting certain references, including the one noted by Pierre Febvre and others to which the Council has given consideration. This firm also noted that it was evident that the therapeutic action of their particular product [potassium guaiacol sulfonate] has not, and probably cannot, be explained satisfactorily on a laboratory basis, but that clinical observations speak of definite beneficial effects produced by such preparations.

The Council has taken full cognizance of the fact that the Maltbie Chemical Company instituted experimental and pharmacologic studies and is planning actual clinical tests but at the same time notes that other firms are not sufficiently interested in the products to take similar action, nor have they submitted anything in their correspondence with the Council which would warrant the Council's giving further consideration to the matter.

V. SUMMARY

1. Reference to reliable textbooks of pharmacology and therapeutics does not indicate the therapeutic value of these preparations.

2. The current literature has nothing to offer that changes the opinions expressed in these textbooks.

3. A survey of clinical experience with the drugs indicates that they are little used by leaders in the profession and that their rationale is little understood by those who do employ them.

4. Consideration of other matters, including the attempts of the A. M. A. Chemical Laboratory to set adequate standards, and the communications with the manufacturers have not produced up to the present any significant evidence of the value of these preparations.

5. In conclusion the Council wishes to note that consideration of evidence in the pharmacologic and medical literature, past and present, as well as a survey of clinical opinion and manufacturers' special pleadings do not indicate that this group of drugs is a necessary part of a modern therapeutic armamentarium.

The Council therefore voted that Calcreose, Calcreose Tablets, 4 grains; Compound Syrup of Calcreose, and Solution Calcreose, sold by the Maltbie Chemical Company; Benzosol, Creosotal-Winthrop, Duotal and Duotal Tablets, 5 grains, sold by the Winthrop Chemical Company, Inc.; Proposote, Proposote Capsules, 5 minims, and Proposote Capsules, 10 minims, sold by Parke, Davis & Co.; Thiocol-Roche, Syrup Thiocol-Roche, and Thiocol-Roche Tablets, 5 grains, and Guaiacol Sulphonate-Merck be omitted from New and Nonofficial Remedies because they are marketed without satisfactory evidence that they have sufficient therapeutic value to justify their retention in N. N. R. In the event of the appearance of evidence of the therapeutic value of this group of compounds, the Council will give it consideration.

The following are the letter and questionnaire referred to earlier as sent to the members of the Association of American Physicians and the American Pediatric Society:

"The Council on Pharmacy and Chemistry has under consideration the question whether or not acceptance of certain guaiacol and creosote preparations for oral administration should be continued in New and Nonofficial Remedies. The preparations are the following:

Calcreose (calcium creosotate)
Creosotal (creosote carbonate)
Benzosol (guaiacol benzoate)
Duotal (guaiacol carbonate)
Proposote (creosote phenylpropionate)
Thiocol (potassium guaiacolsulfonate)

"Examination of the literature within the last ten years failed to indicate any carefully controlled evidence of the value of these preparations. On the other hand, there are clinicians

who continue to use these preparations. In order that the Council may be in better position to make a decision, it has authorized that a questionnaire be sent to members of the Association of American Physicians and the American Pediatric Society.

"It will be appreciated therefore if you will kindly answer the questions contained on the enclosed postcard and sign your name. We shall be glad to have you expand your remarks in a letter if you feel so inclined. As is usual with such requests of the Council, your name will not be used."

The postcard questionnaire:

1. Do you prescribe preparations of guaiacol and creosote for internal use?..... Often?..... Occasionally?..... Rarely?..... Never?.....
2. If so, for what purposes do you prescribe them?.....
3. Have you any convincing evidence that they are really effective in these conditions?.....
4. Have you conducted any blind test of these substances or do you know of any such blind tests?.....
5. Has your use of these substances increased or decreased?.....
6. Further remarks: .....

Council on Foods

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION AND WILL BE LISTED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED.

FRANKLIN C. BING, Secretary.

CELLU THOMPSON SEEDLESS GRAPES PACKED IN WATER

Distributor.—The Chicago Dietetic Supply House, Inc., Chicago.

Packer.—Hunt Brothers, San Francisco.

Description.—Canned cooked Thompson Seedless Grapes packed in water without added sugar or salt.

Manufacture.—Selected Thompson Seedless Grapes from the San Joaquin Valley, Calif., are stemmed by hand, sorted for size (only the largest size is used in this pack), washed and placed in the cans by hand. The cans are weighed, filled with water, heated for six minutes at 91 C., sealed and processed at 100 C. for nineteen minutes. A sulfur dust or liquid is applied prior to or during the blossoming period.

Analysis (submitted by manufacturer).—Moisture 88.5%, total solids 11.5%, ash 0.2%, fat (ether extract) 0.7%, protein (N × 6.25) 0.4%, invert sugar 9.8%, sucrose 0.05%, crude fiber 0.16%, carbohydrates other than crude fiber (by difference) 10.0%.

Calories.—0.48 per gram; 14 per ounce.

ARTISANA DISTILLED WATER

Manufacturer.—Artisana Water Company, Phoenix, Ariz.

Description.—Distilled water practically free of micro-organisms.

Manufacture.—Water issuing at a constant temperature of 23 C. from an artesian well 392 feet deep, encased its entire length with standard screw type steel casing, is pumped through a closed system into hydropneumatic tanks and automatically fed into the boiler of a still having a capacity of 30 gallons per hour. The well water is distilled, passed through copper pipes to a copper reservoir, and immediately filled into clean five-gallon glass bottles. The cork and bottle neck are covered with a dust-proof paper cap. All water so bottled is delivered within twenty-four hours. The boiler is thoroughly cleaned each day before firing. The first run of from 15 to 20 gallons of water is discarded.

Analysis (submitted by manufacturer).—*Sanitary analysis:* sediment none, turbidity none, odor none, color none, total solids 4.0. *Parts per million:* Nitrogen as: free ammonia 0.08, total organic 0.31, nitrites 0.000, nitrates 0.000; oxygen consumed 0.000; total chlorine 0.000; hardness (soap method) 2.0.

Micro-Organisms (data submitted by manufacturer).—Total bacteria per cubic centimeter: at 20 C. less than 1, at 37 C. less than 1. No evidence of the presence of organisms of the B. coli group.

(1) FARMFRESH EVAPORATED MILK
(2) RIECK'S PRIVATE BRAND EVAPORATED MILK

Manufacturer.—Rieck-McJunkin Dairy Company, Pittsburgh.

Description.—Unsweetened, sterilized, evaporated milk.

Manufacture.—Milk from company and government inspected farms is tested, preheated, evaporated under vacuum, homogenized, cooled, again filtered, filled into cans, sealed and sterilized.

Analysis (submitted by manufacturer).—Moisture 73.6%, total solids 26.4%, ash 1.6%, fat (ether extract) 7.8%, protein (N × 6.38) 6.8%, lactose (by difference) 10.2%, acidity 0.35%.

Calories.—1.4 per gram; 40 ounce.

GERBER'S STRAINED APRICOT AND APPLE SAUCE

Manufacturer.—Gerber Products Company, Fremont, Mich.

Description.—Canned sieved mixture of peeled cooked apricots and unpeeled cooked apples, slightly sweetened.

Manufacture.—Selected fully ripened apricots are sorted, peeled, pitted, steamed, packed into cans and heat processed. Apples are cleaned by washing in diluted hydrochloric acid and rinsing thoroughly in water. They are then sorted, cored and steamed. Formula proportions of the canned apricots and the steamed apples are mixed, sieved, slightly sweetened to maintain uniform sweetness, filled into cans, sealed and heat processed.

Analysis (submitted by manufacturer).—Moisture 82.5%, total solids 17.5%, ash 0.5%, fat (ether extract) 0.2%, protein (N × 6.25) 0.5%, crude fiber 0.4%, carbohydrates other than crude fiber (by difference) 16.0%, calcium (Ca) 0.009%, phosphorus (P) 0.016%, iron (Fe) 0.0014%, titratable acidity (expressed in terms of citric acid) 0.65 Gm. per hundred grams.

Calories.—0.7 per gram; 20 per ounce.

Vitamins.—Feeding tests have shown that this product is an excellent source of vitamin A and contains significant amounts of vitamin B_1.

CELLU BRAND KADOTA FIGS PACKED IN WATER

Distributor.—The Chicago Dietetic Supply House, Inc., Chicago.

Packer.—Kings County Packing Company, Armona, Calif.

Description.—Canned cooked Kadota figs packed in water without added sugar or salt.

Manufacture.—Uniform Kadota figs are sorted, washed, placed in cans and covered with water. The cans are heated to 88 C., sealed and processed for sixty minutes at 100 C. Trees are sprayed before the leaves or fruit appear.

Analysis (submitted by manufacturer).—Moisture 87.5%, total solids 12.5%, ash 0.4%, fat (ether extract) 0.05%, protein (N × 6.25) 0.5%, invert sugar 8.8%, sucrose 0.7%, crude fiber 0.75%, carbohydrates other than crude fiber (by difference) 10.8%.

Calories.—0.46 per gram; 13 per ounce.

SOUTHERN MAID OLEOMARGARINE

Manufacturer.—The Cudahy Packing Company, Chicago.

Description.—Margarine prepared from refined hydrogenated deodorized cottonseed oil, salt, pasteurized cultured skim milk and an emulsifying agent, a derivative of glycerin. Contains 0.1 per cent of sodium benzoate.

Manufacture.—Refined hydrogenated deodorized cottonseed oil is warmed and churned with pasteurized cultured skim milk, salt and a derivative of glycerin. Sodium benzoate is added. The resulting emulsion is solidified by contact with ice cold water, refrigerated, automatically molded, wrapped and packed in cartons.

Analysis (submitted by manufacturer).—Moisture 15.0%, total solids 85.0%, ash 2.7%, sodium chloride (NaCl) 2.6%, fat (ether extract) 81.4%, protein (N × 6.25) 0.4% and carbohydrates (by difference) 0.5%.

Calories.—7.36 per gram; 209 per ounce.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JANUARY 15, 1938

MEDICAL CARE FOR ALL THE PEOPLE

Under the leadership of many county medical societies, with the approval of the state medical societies and in accordance with the actions of the House of Delegates of the American Medical Association, definite provisions for medical service to the indigent and to those partially able to pay have already been established in various parts of the country. Hundreds of such plans have been reported to the Bureau of Medical Economics of the American Medical Association and many of them have been described from time to time in considerable detail in the Organization Section of THE JOURNAL. In the state of Pennsylvania seventeen counties now have such plans actively in effect. In the state of Iowa many county medical societies have taken over completely the medical care of the indigent. In Kansas, in California, in Michigan, in Missouri and in many other states, plans already functioning seem to have solved to a large degree the question of preventive medicine and medical care for the people covered by these plans.

At its annual session in June 1937 the American Medical Association reaffirmed its willingness to do its utmost today, as in the past, to provide adequate medical service for those unable to pay either in whole or in part for medical care. At that time the American Medical Association also officially reaffirmed its willingness, on receipt of direct request, to cooperate with any governmental or other qualified agency and to make available the information, observations and results of investigations together with any facilities of the Association. The Social Security Board, the United States Public Health Service, the bureau devoted to maternal and child welfare in the Department of Labor, and many other government bureaus, commissions and agencies are known to be engaged in studies of health services which may yield information of importance in planning for the future. Thus far no call has come from any governmental agency for the cooperation of the American Medical Association in studying the need of all or of any groups of people for medical service, or to determine to what extent any considerable proportion of our public are suffering from lack of medical care.

At the meeting of the American Public Health Association, held a few months ago in New York City, an address was made by Miss Josephine Roche, third assistant secretary of the treasury and in charge of the United States Public Health Service, in which she emphasized to that organization the importance of determining and meeting as soon as possible the actual needs of the indigent and of those partially indigent in relationship to medical care. Moved perhaps by her appeal, the American Public Health Association appointed a committee to confer with the Board of Trustees and the officers of the American Medical Association with a view to stimulating medical organizations everywhere toward greater activity in this matter. That committee met with the Executive Committee of the Board of Trustees of the American Medical Association in Chicago late in December. As a result of that conference the following resolutions were adopted by the Board of Trustees:

WHEREAS, A varying number of people may at times be insufficiently supplied with needed medical service for the maintenance of health and the prevention of disease; and

WHEREAS, The means of supplying medical service differ in various communities; be it

Resolved, That the American Medical Association stimulate the state and county medical societies to assume leadership, securing cooperation of state and local health agencies, hospital authorities, the dental, nursing and correlated professions, welfare agencies and community chests in determining for each county in the United States the prevailing need for medical and preventive medical service where such may be insufficient or unavailable; and that such state and county medical societies develop for each county the preferable procedure for supplying these several needs, utilizing to the fullest extent medical and health agencies now available, in accordance with the established policies of the American Medical Association. Be it further

Resolved, That the Board of Trustees of the American Medical Association establish a committee to cooperate with the Bureau of Medical Economics in outlining the necessary procedures for making further studies and reports of the prevailing need for medical and preventive medical services; and that the Secretary of the American Medical Association arrange to develop such activities through the secretaries of state and county medical societies in each instance, urging the formation of special committees in each county and state where committees are not available for this purpose.

The undertaking proposed by this resolution is an attempt to apply on a nation-wide scale the best features of the numerous plans already in effect, utilizing in each county to the fullest extent the resources there available. Thereby it becomes possible for the organization to act specifically as a clearing house in the initiation, development and functioning of what may well evolve into a comprehensive system of medical care for all the people according to the American plan of medical practice.

THE COMMONWEALTH FUND

In 1918 Mrs. Stephen V. Harkness gave $10,000,000 to establish the Commonwealth Fund. Subsequent donations have increased the endowment to a total of about $50,000,000, including $8,000,000 recently given by Edward S. Harkness, president of the Commonwealth Fund. These large sums have been dedicated to general philanthropic purposes without permanent restrictions. For the present, however, the income from $3,000,000 of the recent gift will be used for the development of rural hospitals, and the income from the other $5,000,000 for medical education and research.

The building of rural hospitals is not a new venture with the Commonwealth Fund, for it has already made possible ten hospitals in rural districts: two in Tennessee and one each in Maine, Ohio, Virginia, Kentucky, Mississippi, Oklahoma, Kansas and Utah. Eight of these are already in operation; another is nearing completion, and the tenth, in Provo, Utah, is still in the blueprint stage. The Commonwealth Fund plans to build one new rural community hospital annually.

A community hospital, as defined by the fund,[1] is one that serves the whole community regardless of race, color, creed or economic conditions. It is a place where the community provides for the care of its own sick by its own physicians and nurses, and it is owned by the people who expect to use it. While the doors of the community hospitals are open to all reputable physicians, the privilege of doing certain kinds of work, particularly major surgery, is to be earned only by adequate preparation. The community hospital puts a laboratory and an x-ray technician at the service of the physician and provides constant care for patients under a physician's direction. It also gives these physicians an organization through which relations can be maintained with consultants in large teaching centers.

The Commonwealth Fund has assisted in providing community hospitals in the belief they will attract well trained young physicians to these rural communities to practice. As a further means of helping in this movement, the fund has provided scholarships at Vanderbilt, Tulane and Tufts medical schools for young men who would agree to practice for a term of years in rural communities in Tennessee, Mississippi or Massachusetts. Eighteen young physicians are now established in practice under this plan, and fifty young physicians have settled in the vicinity of the first six community hospitals.

The type of young physician so trained is he who does his own blood counts, stool examinations, smears and urinalyses. He uses laboratories for cultures and Wassermann tests. He keeps within reasonable range of new methods of treatment and technics but is cautious lest they involve risks which endanger his patient and his reputation. These young physicians see all comers. They meet what the day brings. They lance boils, treat colds, make spinal punctures and perhaps type the pneumococci present in pneumonia patients. The community hospitals have well equipped fireproof buildings of about fifty beds. They place an emphasis on good care of patients, careful records, staff discussion, graduate study and competent consultation.

The Commonwealth Fund has provided more than 400 fellowships for older physicians in practice who wish to brush up on recent advances. The older physicians have been enabled to study from one to four months at Harvard, Vanderbilt, Tulane and other medical schools. Assistance has been given at Tulane in financing a medical extension division which has made available neighborhood courses for physicians throughout the state of Mississippi.

The fund has aided medical schools in more general ways. It has aided in expanding the department of pediatrics at Tulane, has helped build facilities for teaching psychiatry as an element in general medicine at the University of Louisville and has helped to finance teaching clinics in which emotional and behavior problems are duly considered in the care of children's diseases at Cornell, Columbia and Harvard. The fund has provided fellowships for graduate study in psychiatry at the University of Colorado and at Johns Hopkins, and for special graduate training of psychiatrists at five child guidance clinics. However, after being actively interested in the establishment of child guidance clinics in the United States for years, the fund in 1927 ceased to give direct aid to such clinics generally, although it still shares part of the cost of the London Child Guidance Clinic in England and supports the educational work of the Child Guidance Council.

Among other endeavors, the Commonwealth Fund has encouraged research in medical schools and hospitals. In allocating the new income made available for this purpose, the fund will seek only research projects that promise to contribute to better medical practice. During the last year seven research undertakings were selected for subsidy in addition to a number carried forward from previous years. Among the seven research problems selected are the study of preeclamptic toxemia, eclampsia, the pernicious vomiting of pregnancy and the communicable infections associated with childbirth and abortion, at the New York University College of Medicine; a study of the nature of various infections of the central nervous system, of poliomyelitis, at Johns Hopkins School of Medicine; studies on clinical and immunologic phases of poliomyelitis at Harvard University Medical School; a comparative study of certain virus infections at Washington University School of Medicine at St. Louis, as a step toward better knowledge of the virus of trachoma, and the testing

1. Summary of the Nineteenth Annual Report of the Commonwealth Fund for the Year Ending September 30, 1937.

of certain methods of treatment suggested from work already done on this virus. The fund has sponsored statistical and clinical studies of maternal mortality in New York and in two southern counties, has sponsored a study of disorders of pregnancy and childbirth at New York University, has helped finance extension courses in obstetrics for physicians in three states, has provided facilities for the safeguarding of childbirth in its rural hospitals, and has built up maternity nursing in rural health departments.

In the field of public health, the Commonwealth Fund believes that an especial current need is for technical experimentation to refine methods and gradually to raise standards. It is aiding, therefore, in experimental activities in Tennessee and Mississippi, where the state health departments have been strengthened by providing traveling units which advise local health departments and improve their methods of work. One county in each of these two states has been selected for a demonstration of adequate public health service, Sumner County in Tennessee and Jones County in Mississippi having begun demonstration programs during the last year. Four other counties where similar work had been done for several years have assumed responsibility for maintaining their health departments without further aid from the fund.

While much emphasis has been placed on activities in the field of health and medical education, other activities have received aid. In fact, the broad terms of this philanthropy make the income or principal applicable to any object which is considered "for the welfare of mankind."[2] Each year a portion of the income is reserved for grants to projects for which it assumes no administrative responsibility. Grants are occasionally made for other social, philanthropic and educational purposes.

There is a Legal Research Committee associated with the fund which sponsors studies in administrative law and the history of local concepts. It has aided in the completion of a five volume study of the Interstate Commerce Commission. The fund has a plan whereby a group of British students come to the United States each year for study and travel as guests of the fund. It provides for three fellows appointed from the Home Civil Service of the British government, and they come to the United States on leave of absence for a year from their government positions to study and observe. Thirty-one other fellows appointed from British universities or from the government service will spend two years in the United States and will travel widely during the coming summer.

Thus it appears that much wisdom and nobility of purpose have been manifest not only in the original conception of the Commonwealth Fund but likewise throughout the many years of its administration.

2. Commonwealth Fund. American and Canadian Hospitals. Chicago: Physicians' Record Company, 1937, page 68.

Current Comment

ANNUAL DUES NOW PAYABLE

Physicians who have not yet sent in their annual Fellowship and subscription dues for 1938 will find it convenient to utilize the colored slip in this issue of THE JOURNAL. Properly folded, it forms a safe, postage-prepaid envelop. All that is necessary is to make a few notations on the slip and mail with check, draft or money order. Note that along with THE JOURNAL are listed the subscription prices of the special journals published by the Association and also *Hygeia*, the Health Magazine. One order and one remittance can cover all subscriptions for the coming year. Fellows and subscribers who have already remitted will, of course, disregard the colored slip.

DON'T GAMBLE WITH GAMBLE

Recently several physicians have paid $15 each for a listing of their names in an insurance medical directory; apparently they understood that they would be selected as medical examiners for certain insurance companies. This proposition was presented by one Mr. C. H. Gamble, representing the National Claims Statistical Bureau with offices in New York City and Atlanta, Ga. In the event that one does not like the name of this organization, Mr. Gamble also represents the INsurOR INternationAL Association and the INsurOR Statistical Bureau with offices reported to be in Washington, D. C., Chicago, Memphis, Oakland, Calif., and Dallas, Texas. Letters mailed to several of these addresses were returned marked "Name not in city directory." Inquiries sent to the Better Business Bureaus in these cities also failed to locate any such organizations. Although Mr. Gamble uses a number of addresses in a great many cities, evidently his office is "under his hat." Physicians throughout the length and breadth of the United States have been visited by Mr. Gamble. From South Carolina to California, from Illinois to Louisiana, from Florida, Texas and Arizona have come complaints by physicians that the $15 paid out resulted in absolutely nothing—not even a press proof of their names. Apparently, Mr. Gamble has been too busy traveling to work up the rest of his business. Twice during 1937 THE JOURNAL published articles on insurance medical directories,[1] pointing out the inadvisability of paying a fee for a listing in such directories. A resolution approved by the Judicial Council and adopted by the House of Delegates has condemned the listing of physicians in directories published by commercial con-

1. Medical Directories, J. A. M. A. **108**: 25B (Jan. 23) 1937; Why Pay a Fee? ibid. **109**: 23B (Sept. 4) 1937.

cerns as unethical solicitation of patients. Officials of insurance companies have indicated clearly that commercial insurance medical directories are not used in the selection or appointment of physicians as examiners. Maybe some doctors have to pay for experiences of this kind, but reading THE JOURNAL is cheaper—and you get scientific articles also!

FRIEDLÄNDER BACILLUS PNEUMONIA

The reported incidence of the Friedländer bacillus as the causative agent in pneumonia varies. The organism has been found also in chronic pulmonary abscess, influenza, empyema and miscellaneous infections of the bronchial tree and larynx. The pathogenicity in man, however, is not limited to the respiratory tract. Bullowa and his colleagues[1] have reviewed forty-one cases of this form of pneumonia at the Harlem Hospital fairly evenly distributed over a seven year period with the exception of November 1935, during which month there were five cases, all beginning within a span of a few days. The diagnosis of pneumonia in all the cases was made by clinical and roentgenographic study, and the Friedländer bacillus was recovered either from the blood or by pulmonary suction, or both, as well as from the sputum. The organisms were identified and typed. Of the entire group of forty-one patients, thirty-six were men, ten of whom were white men and twenty-six were Negroes. All five women were Negresses. Such predisposing factors as alcoholism and trauma were only occasionally present. Approximately half of the patients contracted the disease with the suddenness characteristic of pneumococcic lobar pneumonia. Profound and rapidly progressive prostration was characteristic. In two thirds of the patients the sputum did not differ materially in appearance from that seen in pneumococcic pneumonia. The course of the illness was not marked by any unusual preponderance of extrapulmonary manifestations. The rapid dissolution was clinically characteristic. The blood count varied between polymorphonuclear leukocytosis and the frequently described leukopenia, the latter being found in approximately one third. Thirty-four patients, or 83 per cent, of the entire group died. Necropsy was performed on ten patients. The predominant lesion was a massive lobar consolidation with a viscid, gelatinous exudate. Specific serum therapy with Friedländer bacillus type A antiserum was attempted on eight patients. Omitting two patients, there were six who were treated with specific serum and thirty-five who were not so treated. Thirty of the patients not given serum died. Three of the six patients with infections due to the type A Friedländer bacillus who received specific serum therapy also died. The highest mortality of the whole group (94 per cent) occurred in patients infected with the type A Friedländer bacillus who were not given serum.

1. Bullowa, J. G. M.; Chess, Joseph, and Friedman, N. B.: Pneumonia Due to Bacillus Friedländeri, Arch. Int. Med. 60: 735 (Nov.) 1937.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—The northwestern division of the Medical Association of the State of Alabama will be addressed in Tuscaloosa, January 21, by Drs. George T. Pack, New York, on "Indications for Surgery and Radiation Therapy in the Treatment of Cancer"; Marye Y. Dabney, Birmingham, "Sterility"; Ralph McBurney, University, "Ptomaine Poisoning, a Misnomer"; Ivan C. Berrey, Birmingham, "The Irritable Colon," and Erskine M. Chenault, Decatur, "Skin Grafting as an Office Procedure." Visits will be made to the Bryce Hospital, Partlow School and Veteran's Administration Facility.

CALIFORNIA

Personal.—The San Francisco County Medical Society adopted a resolution December 14 honoring Dr. Douglass W. Montgomery, who has completed more than fifty years in the practice of medicine. Dr. Montgomery was president of the American Dermatological Association in 1910.

New Course in Medical Stenography.—A free course in medical reporting for stenographers has been established at the Evening High School of Commerce, San Francisco, with Dr. Harry M. Elder, a practicing physician, in charge. The course is open to persons who already have stenographic training and is designed to give them a thorough working knowledge of medical and surgical terms. Classes will meet Monday and Wednesday evenings from 7 to 9. The first hour will be devoted to informal discussions of the problems of the medical profession and its fight against disease. The problems of such diseases as syphilis, cancer, tuberculosis and infantile paralysis will be presented. There will be a brief study of the fundamental structure and functions of the major organs in their relation to health and disease. The danger of using "patent medicines" and nostrums and of consulting quacks in the diagnosis and treatment of diseases will be stressed. The second hour will consist of dictation on these subjects by Dr. Elder.

ILLINOIS

Personal.—Dr. Loran E. Orr, formerly of Greenview, has been appointed coordinating epidemiologist to the state department of health, Springfield, according to the *Illinois Health Messenger*. —— Dr. Andrew F. Barnett, Hines, has been appointed managing officer of the Anna State Hospital, succeeding the late Dr. Ralph A. Goodner.

Lectures for Nurses at Hines Hospital.—A series of lectures for the nursing staff of the Edward Hines Jr. Hospital, Hines, began January 11 under the auspices of the Chicago Tuberculosis Institute. Dr. Meyer Solomon gave the first lecture, on "Mental Health and Tuberculosis." Other lecturers include the following Chicago physicians:

Dr. Hugo O. Deuss, Treatment of Pulmonary Tuberculosis, January 18.
Dr. Paul A. Teschner, assistant director, Bureau of Health and Public Instruction, American Medical Association, The Nurse of Today, January 25.
Dr. Franklin R. Fitch, Gonorrhea and Syphilis—Twin Public Health Problems, February 1.
Dr. Jerome R. Head, Childhood Type of Tuberculosis, February 8.
Dr. Robert S. Berghoff, The More Common Forms of Heart Disease, February 15.

Chicago

Dr. David to Give Lewis Linn McArthur Lecture.—Dr. Vernon C. David, chairman of the department of surgery, Rush Medical College, will deliver the fourteenth Lewis Linn McArthur Lecture of the Frank Billings Foundation at the Institute of Medicine of Chicago, January 28; his subject will be "A Consideration of Some Etiological and Pathological Factors in Cancer of the Large Bowel."

Past Presidents to Honor Dr. Kearsley.—Dr. Mary Jeannette Kearsley will be guest of honor at a dinner January 19 given by the past presidents of the Aux Plaines Branch of the Chicago Medical Society in recognition of her completion of fifty years in the practice of medicine. Dr. Morris Fishbein, Editor of THE JOURNAL, will be the principal speaker at the dinner. Dr. Kearsley is the only woman thus far to be president of the branch society.

Tuberculin Distribution Service.—The Chicago Tuberculosis Institute January 1 began distribution of tuberculin to physicians of Chicago and Cook County. On request from a physician, either by telephone or by letter, the institute will send by return mail a supply of first and second strength purified protein derivative sufficient for ten skin tests. Included will be a card on which additional requests may be made when the supply on hand is exhausted or becomes old. There is no charge for the service. The institute hopes in this manner to facilitate tuberculin skin testing as an aid to early diagnosis of tuberculosis.

Joint Maternal Welfare Committee.—At a meeting of seven medical and hospital societies at the Union League Club, December 16, the Joint Maternal Welfare Committee of Cook County was organized to maintain the highest possible standards for medical and hospital care of new-born infants and maternity patients. The committee is composed of representatives of the Chicago Gynecological Society, the Chicago Medical Society, the Chicago board of health, the Chicago Hospital Council, the Chicago Hospital Association, the Infant Welfare Society of Chicago and the diocesan Catholic hospitals, according to the Chicago *Tribune*. Dr. Fred L. Adair, chief of staff of the Chicago Lying-In Hospital, was elected chairman, and Arnold F. Emch, director of the Chicago Hospital Council, was appointed executive secretary.

Society News—Dr. Frank to Lecture.—The Chicago Medical Society and the Chicago Gynecological Society will be addressed at the Goodman Theater January 19 by Dr. Robert T. Frank, New York, on "The Sex Hormones: Their Physiological Significance and Use in Practice."——The Chicago Pathological Society was addressed January 10 by Dr. William H. Sweet, among others, on "Toxic Changes in the Spinal Cord Resulting from Spinal Anesthesia."——A symposium on lymphoblastoma was presented before the Chicago Roentgen Society January 13 by Drs. Sol R. Rosenthal, Louis R. Limarzi, Ford K. Hick, Adolph Hartung and Theodore J. Wachowski, all members of the faculty of the University of Illinois School of Medicine.——Dr. Cecil S. O'Brien, Iowa City, will discuss "Staphylococcic Conjunctivitis" before the Chicago Ophthalmological Society January 17.——The Chicago Gynecological Society was addressed December 17 by Drs. Ralph A. Reis and Sidney D. Mesirow on "Studies in the Evaluation of Mammography"; David S. Hillis and Solomon J. Benensohn on "Infant Mortality in 16,000 Deliveries at the Cook County Hospital"; William H. Rubovits, Emanuel Taft and Frank Neuwelt, "Importance of Pathological Properties of Meconium in Relation to Cesarean Section."——Dr. Ralph K. Ghormley, Rochester, Minn., among others, addressed the Chicago Orthopaedic Society December 10 on "Some Unusual Lesions of Vertebrae."——Dr. George E. Wakerlin, among others, addressed the Chicago Society of Internal Medicine, December 20, on "Bio-Assay of the Hemopoietic Liver Principle."

KANSAS

Medical Library Reopened.—The medical library at St. Francis Hospital, Wichita, which was closed in 1929, has been reopened. A new room for periodicals has been provided, in which thirty current periodicals are available. Voluntary contributions of a library club furnish the journals. The library is open to all members of the profession.

LOUISIANA

Lectures on Pediatrics.—The state board of health and the committee on medical education of the state medical society have organized a series of courses on pediatrics to be conducted in all councilor districts with the exception of the first and second districts, according to the *New Orleans Medical and Surgical Journal*. The first course opened in the seventh district with the following speakers: Drs. Robert A. Strong, December 6-10, Lake Charles; Roy E. de la Houssaye, December 13-17, Opelousas, and Jack E. Strange, January 10-14, Crowley. Three courses, each consisting of a daily lecture for five consecutive days, were conducted in each district in designated centers.

MARYLAND

Birth and Death Rates.—In 1936 there were 26,588 births and 21,960 deaths in Maryland, giving rates of 15.9 and 13.1 per thousand of population, respectively. These rates correspond with 27,236 births and a rate of 16.3 in 1935 and 21,182 deaths with a rate of 12.7. The infant mortality rate was 69.1 per thousand live births, while the maternal mortality rate was 4.7 as compared with 62 and 5.4 respectively in 1935. The death rate for tuberculosis was 85.2 per hundred thousand of population, cancer 128.1 and motor vehicle accidents 27.6, diseases of the heart 304.5, bronchopneumonia 50.7, other forms of pneumonia 59.1, alcoholism 2.9, and suicide 14.9.

Transactions of International Congress of Hygiene.—The state health department of Maryland has a limited number of the Transactions of the Fifteenth International Congress on Hygiene and Demography meeting in 1912, which it will be glad to distribute without cost to any physician, public health official or library desiring a set. The set consists of six volumes dealing with the following subjects: Organization and Membership, Proceedings of the Joint Sessions and General Index; Hygienic Microbiology and Parasitology; Dietetic Hygiene; Hygienic Physiology; Hygiene of Infancy and Childhood; School Hygiene; Hygiene of Occupations; Control of Infectious Diseases; State and Municipal Hygiene; Hygiene of Traffic and Transportation; Military, Naval and Tropical Hygiene and Demography. Applications should be sent to Dr. Robert H. Riley, director of the state department of health, 2411 North Charles Street, Baltimore. The sets will be sent with express charges collect.

MASSACHUSETTS

Boston University Receives $100,000.—Dr. and Mrs. J. Emmons Briggs, Boston, have given $100,000 to the Boston University School of Medicine. The gift includes their residence at 477 Beacon Street, which will be converted into a dormitory, according to the Boston *Post*. Dr. Briggs is professor emeritus of surgery at Boston University and has been a trustee of the university for many years.

MICHIGAN

Fund for Research on Arthritis.—The fund of $10,000 to finance a study of rheumatism at the University Hospital, Ann Arbor, recently made available by the Horace Rackham Fund, has been increased, according to the *University Hospital Bulletin*. The project will now have available the interest from a million dollar endowment, which is to be used annually for not less than five and not more than ten years. Should research on arthritis be completed, any other major problem of medical research may be selected by the executive board of the graduate school of the university.

Annual Secretaries' Conference.—The Michigan State Medical Society will hold its annual secretaries' conference at the Olds Hotel, Lansing, January 23, with Dr. Leland E. Holly, Muskegon, as chairman. Speakers will include:

Lawrence C. Salter, medical editor, *Detroit Free Press*, Public Relations by the County Medical Society.
Dr. Martin H. Hoffmann, Eloise, How to Achieve Maximum Membership.
Dr. Allan W. McDonald, Detroit, Medical Practice.
Dr. Charles B. Wright, Minneapolis, trustee of the American Medical Association, Medicine in the Front Line Trenches.
George T. Gundry, auditor general of Michigan, Problems of Administering the Afflicted Child Law.
Dr. L. Fernald Foster, Bay City, secretary, state medical society, What's Going On in Michigan.

A round table discussion on preventive medicine, with Dr. Don W. Gudakunst, newly appointed state health commissioner, as chairman, will conclude the session. Speakers will be Drs. Osborne A. Brines, Detroit, cancer; Edgar E. Martmer, Detroit, immunization; Alexander M. Campbell, Grand Rapids, maternal health; Henry A. Luce, Detroit, mental hygiene; Ledru O. Geib, Detroit, preventive medicine; Robert S. Breakey, Lansing, syphilis, and Bruce H. Douglas, Detroit, tuberculosis.

MINNESOTA

Physical Education for Women.—Required physical education courses for college women appear to be justified by improvements in physical control and better attitudes toward health and physical activity, according to a study made at the University of Minnesota. A group of 368 entering freshmen participated in the regular required courses in physical education; 347 were not permitted to take part in any of the required classes, and the results in the two groups were compared.

MISSISSIPPI

Society News.—At a meeting of the South Mississippi Medical Society, December 8, Drs. Gilbert C. Anderson spoke on "Management of Head Injuries"; Shirley C. Lyons, "Early Diagnosis and Treatment of Empyema," and John T. Sanders, "Management and Diagnosis of Sterility"; all are of New Orleans.

New Director of Maternal and Child Health Division.—Dr. John A. Milne, director of the field unit for the state board of health, has been appointed director of the maternal and child health division, newspapers reported. Dr. Milne will take over a position which Dr. Felix Underwood has held together with his activities as state health officer. Although Dr. Underwood continued as director of maternal and child health after his appointment as state health officer in 1924, it was stated, he never received the salary available for the position. The expansion of the maternal and child health program in the state now demands a full time director, it was said. Aged 37, Dr. Milne graduated at the Dalhousie University Faculty of Medicine, Halifax, N. S., in 1924. Dr. Hugh B. Cottrell, Indianola, since 1935 director of the Sunflower County Health Department, will succeed Dr. Milne as director of the field unit, which supervises the programs of the county health units. Dr. Charles R. Gillespie, Natchez, health officer of Adams County, will take the position in Sunflower County, and Dr. Andrew Hedmeg, formerly of Lexington, will succeed Dr. Gillespie.

MISSOURI

Society News.—Dr. Willard Bartlett and his sons, Drs. Willard Jr. and Robert W. Bartlett, addressed a meeting of the St. Louis Medical Society on goiter recently. A symposium on allergy was presented before the society December 7 by Lloyd R. Jones, Ph.D., and Drs. Carliss Malone Stroud and Charles H. Eyermann.——The Chariton County Medical Society was addressed in Rothville November 17 by Drs. August A. Werner and Ralph L. Cook, St. Louis, on "Clinical Application of Pituitary and Ovarian Hormones in Regard to Uterine Function" and "Children's Diseases of Infectious and Contagious Types" respectively.——At a meeting of the Randolph-Monroe Counties Medical Society in Moberly, November 9, Drs. Charles F. Sherwin and Paul C. Schnoebelen, both of St. Louis, spoke on surgical treatment and x-ray examination, respectively, of cancer of the stomach and the esophagus.——Among others, Dr. John E. Wensley, Harrisonville, addressed the Cass County Medical Society in Harrisonville, December 9, on "Sulfanilamide: Its Actions and Uses."——The South Central Counties Medical Society was addressed, among others, in Mountain Grove December 9 by Dr. Stanley L. Green, Independence, on "Agranulocytic Angina or Septic Sore Throat."

NEW HAMPSHIRE

Personal—Dr. Andrew J. Oberlander, Reading, Mass., has been appointed physician to the University of New Hampshire, Durham, effective January 3. Dr. George G. McGregor, Durham, was in charge temporarily pending a permanent appointment. A news item in THE JOURNAL, January 1, taken from the Manchester *Leader* of December 4, stated that Dr. McGregor had been appointed to the position.

NEW YORK

Medal Offered by Buffalo University.—The University of Buffalo awards annually a gold medal for work in ophthalmology. Details may be obtained from Dr. Harold W. Cowper, 543 Franklin Street, Buffalo.

Five to Ten Year Study of Influenza.—The Rockefeller Foundation with the cooperation of the Westchester County Department of Health recently announced a field study of influenza to be undertaken immediately and to last from five to ten years in the township of Yorktown in the northern section of the county. The communities of Yorktown Heights, Shrub Oak and other villages including about 1,000 inhabitants will be the study area. These communities were chosen because they are believed to be typical and are relatively isolated from the influence of large cities, there being only a few commuters in them. The project will consist of a medical census followed by a detailed clinical and laboratory investigation of every case of respiratory disease that occurs in the area. A person's work, his health in the past, the type of germ with which he has been stricken and all other data concerning his illness will be recorded. Actual treatment will be left to local physicians, it was pointed out. This study will be unique in that observation will be continuous over several years. It is hoped by this method to obtain information not only about the presence of epidemics but about their absence. The observers can study conditions before, during and after an influenza epidemic if one should strike, it was said. Funds to finance the investigation for eighteen months have been made available, but it is expected that the work will continue several years, according to Dr. Matthias Nicoll, health commissioner of Westchester County.

New York City

Public Lectures at the Academy.—Dr. James J. Walsh will give the next public lecture at the New York Academy of Medicine, the fourth of the current series, January 27, on "Medicine in the Middle Ages." The remaining lectures will be as follows:

Raymond Pearl, Ph.D., professor of biology, Johns Hopkins University, Baltimore, The Search for Longevity, February 27.
Edward E. Free, Ph.D., consulting chemist and physicist, The Physicist's Contribution to Medicine, March 24.
Nicholas Murray Butler, Ph.D., president of Columbia University, Medicine and the Progress of Civilization, April 28.
Dr. Lewis G. Cole, X-Rays Within the Memory of Man, May 26.

Dr. Lewi Honored at Eighty.—Dr. Maurice J. Lewi, president of the First Institute of Podiatry and the Foot Clinics of New York, was honored at a testimonial dinner on his eightieth birthday, December 1, given at the Biltmore Hotel by various friends. Dr. Lewi graduated from Albany Medical College in 1877 and was at one time instructor there in gynecology, and professor of medical jurisprudence at the Albany Law School. He has served as chairman of the committee on medical legislation of the Medical Society of the State of New York, as president of the Medical Society of the County of Albany and as secretary of the New York State Board of Medical Examiners. He is the author of several books on chiropody and podiatry.

Proposed Hospital Budget of Sixty Million.—Dr. Sigismund S. Goldwater, commissioner of hospitals, submitted to the acting director of the budget for the city a proposed budget for his department amounting to $60,851,627 for the nine months beginning April 1. The largest item is for new construction of general and special hospitals at an estimated cost of $33,950,000. These include four new general hospitals to serve certain sections of Brooklyn and Queens whose needs are not now covered by either public or private hospitals, five tuberculosis hospitals or additions to present institutions, one cancer hospital on Welfare Island, one for venereal disease in Brooklyn; a new nurses' home and school for nurses at Bellevue Hospital; a laboratory and morgue at Kings County Hospital and a home for dependents on Welfare Island to replace old buildings. Eight new outpatient departments are urgently needed for work with indigents, now hampered by lack of space and lack of equipment; these are listed separately at an estimated cost of $3,250,000. Urgent relief and expansion projects call for expenditure of $5,620,000 in the commissioner's statement. Appropriations needed to complete construction now under way and to furnish new buildings amount to $16,875,100.

Society News.—Dr. Howard Fox was elected commander of the Caduceus Post No. 818, American Legion, at a recent meeting. Drs. William M. Ford, Conrad Berens and Nelson M. Holden, Brooklyn, were elected vice commanders.——Drs. Stafford L. Warren and Charles M. Carpenter, Rochester, addressed the Medical Society of the County of Kings, December 21, on "Fever Therapy with Special Reference to Gonococcal Infection." The society will give a dinner February 22 in honor of Dr. Charles H. Goodrich, Brooklyn, president of the Medical Society of the State of New York, who is a member of the Kings County society.——Dr. Thomas B. Futcher, Baltimore addressed a meeting of the New York chapter of the National Society for the Advancement of Gastro-Enterology, November 29, on "Causes of Enlargement of the Liver." A symposium on colitis was presented by Drs. Joseph Felsen, Anthony Bassler, Franz J. Lust and Frank C. Yeomans.——Drs. Alvan L. Barach and John Murray Steele will address the New York Heart Association at its annual meeting, January 18, on "Oxygen Therapy in Heart Disease" and "Pulse Wave Velocity" respectively.——Dr. Herbert C. Chase gave an afternoon lecture before the Medical Society of the County of Queens, January 7, on cancer of the breast.

NORTH CAROLINA

Society News.—Drs. Julian M. Ruffin, Durham, and David R. Murchison, Wilmington, addressed the Third District Medical Society in November on "Amebic Dysentery" and "The Electrocardiogram as an Aid in Diagnosis" respectively.——Drs. Porter P. Vinson and Emory H. Anderson, both of Richmond, addressed the New Hanover County Medical Society, Wilmington, December 16, on "Bronchoscopy and Its Use in Treating Lung Diseases" and "Mediastinal Lymphosarcoma with Spontaneous Pneumothorax" respectively.

OKLAHOMA

Premedical Requirements Raised to Three Years.—At a meeting of the board of regents of the University of Oklahoma, January 3, the educational requirements for admission to the school of medicine were raised from two to three years, or ninety college hours exclusive of physical education or military science. The change was made on recommendation of the faculty of the medical school, of which Dr. Robert U. Patterson is dean. The new requirements will become effective with the freshman class to enter next September.

OREGON

Society News.—George E. Burget, Ph.D., addressed the Multnomah County Medical Society, Portland, January 5, on "Some Pathologic Physiology in the Intestinal Tract." Dr. Arthur J. McLean, Portland, addressed the society recently on tumors of the brain.——Dr. Morris L. Bridgeman, Portland, discussed "Practical Knowledge of Pediatrics" before the Central Willamette Medical Society in Albany recently.

PENNSYLVANIA

New County Tuberculosis Hospital.—A new hospital for the treatment of tuberculosis has been completed in Erie County, which will take the place of the Louise Home founded in 1914 near Erie. Dr. Russell S. Anderson, recently on the staff of the Michigan State Sanatorium, Howell, has been appointed superintendent of the new hospital, which has about sixty beds. The Louise Home is to become a preventorium for children between the ages of 4 and 14. The site for the new building was provided by the Erie County Tuberculosis and Health Association.

Academy Award to Bulletin Editor.—The Harrisburg Academy of Medicine has awarded its biennial prize of $500 known as the Seibert Award to Dr. Mathew H. Sherman, editor of the *Dauphin Medical Academician*, for his work in that position. The prize, which must be used for study in Europe, was established twelve years ago in memory of Dr. William H. Seibert by his sister, Miss Catherine Seibert. Dr. Sherman was secretary of the Dauphin County Medical Society from 1931 to 1934 and was named editor of the bulletin in 1935.

Philadelphia

Demonstrations in Otolaryngology.—St. Luke's and Children's Hospital in cooperation with the ear, nose and throat section of the Philadelphia County Medical Society will present a group of graduate and clinical demonstrations at the hospital in the evening of January 20. Sixteen members of the staff will conduct the demonstrations, which will be repeated several times in order to give physicians opportunity to hear and see each one.

Society News.—Speakers at the meeting of the Philadelphia Academy of Surgery, January 3, were Drs. Thomas A. Shallow and Kenneth E. Fry, on "Foreign Bodies Removed from the Intestinal Tract"; John S. Lockwood, "Experiences with Sulfanilamide," and J. Stewart Rodman and Helen Ingleby, "Plasma Cell Mastitis."—— Dr. Ruth Stephenson, among others, addressed the Philadelphia Pediatric Society, December 14, on "A Study of Treatment of Hypochromic Anemia in Infancy."——Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, addressed the Philadelphia County Medical Society at a "Medical Economics Night," January 12, on "Medicine and the National Policy." Dr. Francis F. Borzell, chairman of the society's medical economics committee, spoke on "The County and State Society—A Diagnostic Survey."——Detlev W. Bronk, Ph.D., delivered the seventh Weir Mitchell Oration of the College of Physicians of Philadelphia, January 5, on "The Cellular Organization of Nervous Function."——Drs. I. Charles Lintgen and Kenneth Fry, among others, addressed the Obstetrical Society of Philadelphia, January 6, on "The Sedimentation Rate in the Differential Diagnosis of Acute Appendicitis and Early Pelvic Inflammatory Disease."

Pittsburgh

Society News.—At the meeting of the Allegheny County Medical Society, December 21, the speakers were Drs. George V. Foster, on "The Use of Fascia Lata in the Repair of Hernia"; Lewis E. Etter, Warrendale, "Undulant Fever—Three Cases Treated with Mixed Typhoid Vaccine Intravenously"; Joseph H. Barach, "Medicine in South America." Dr. Gomer S. Llewelyn, Mayview, showed motion pictures of the City Hospital and Home at Mayview.——Drs. William J. Fetter and John P. Griffith addressed the Pittsburgh Surgical Society, December 10, on "Diagnosis and Preoperative Treatment of Hyperthyroidism" and "Surgical Treatment of Hyperthyroidism" respectively.

SOUTH CAROLINA

Symposium on Obstetrics. — The committee on maternal welfare of the South Carolina Medical Association sponsored a symposium on obstetrics at the Columbia Hospital, Columbia, December 8. Drs. Lester A. Wilson, professor of obstetrics, Medical College of South Carolina, Charleston, and Ivan M. Procter, Raleigh, professor of obstetrics, Wake Forest College of Medicine, were the speakers. It was voted that similar meetings should be held about every three months. Dr. Robert E. Seibels, Columbia, is chairman of the maternal welfare committee.

TENNESSEE

Medical Program at Chancellor's Inauguration.—Oliver C. Carmichael, LL.D., dean of the Graduate School and Senior College, Vanderbilt University, Nashville, will be inaugurated as chancellor of the university at a three day ceremony February 3-5 with a symposium on higher education in the South as the principal feature. Isaiah Bowman, Ph.D., president of Johns Hopkins University, Baltimore, will deliver the inaugural address. Part of the symposium will be devoted to medicine with the following speakers:

Dr. William D. Cutter, secretary, Council on Medical Education and Hospitals, American Medical Association, Chicago, Trends in Premedical and Medical Education.
Dr. Irvin Abell, Louisville, Ky., President-Elect of the American Medical Association, Significant Trends in Medical Practice.
Dr. Wilburt C. Davison, dean of Duke University School of Medicine, Durham, N. C., A Survey of Medical Education in the South.
Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., A Forward Look at National Health.

TEXAS

Semicentennial at Houston Hospital.—St. Joseph's Infirmary, Houston, celebrated its fiftieth anniversary December 19. The hospital was founded in 1887 by the Sisters of Charity of the Incarnate Word. In 1895 the building was destroyed by fire and was replaced by the structure that now serves as the administration building. The first laboratory of pathology was established in 1912 and the first x-ray equipment installed in 1921. It now has 207 beds, and a new maternity and children's building is under construction.

Graduate Assembly in San Antonio.—The International Post-Graduate Medical Assembly will be held in San Antonio January 25-27. Mornings will be occupied by general sessions; luncheon meetings will be conducted according to specialty groups and seminars will be offered in the late afternoon. Speakers at the general sessions will be:

Dr. Paul A. O'Leary, Rochester, Minn., Treatment of Early Syphilis.
Dr. Reed M. Nesbit, Ann Arbor, Mich., Pyelitis of Pregnancy.
Dr. Frederick A. Coller, Ann Arbor, Infections of the Face and Neck.
Dr. Franklin B. Bogart, Chattanooga, Tenn., X-Ray Diagnosis of Pulmonary Lesions.
Dr. Eldridge L. Eliason, Philadelphia, Fracture Wrecks.
Dr. Maurice C. Pincoffs, Baltimore, Causes and Consequences of Hemolysis.
Dr. Maurice H. Seevers, Madison, Wis., A Clinical Classification and General Discussion of the Barbiturates.
Dr. Wiley R. Buffington, New Orleans, Interpretation of Vascular Changes in General Sclerosis.
Dr. Frank H. Lahey, Boston, Peptic Ulcer.
Dr. William Boyd, Toronto, Ont., Recent Ideas Regarding the Etiology of Cancer.
Dr. Gordon B. New, Rochester, Minn., What General Practitioners Should Know About the Larynx.
Dr. William P. Healy, New York, Diagnosis and Treatment of the Cervix.
Dr. Mynie G. Peterman, Milwaukee, Muscular Dystrophies.

At the luncheon sessions Dr. Eusebio Guajardo, Monterey, Mexico, will also be a guest speaker. At a public meeting Wednesday evening January 26 Dr. Healy will speak on cancer and Dr. Roscoe R. Spencer, U. S. Public Health Service, Washington, D. C., on syphilis.

WISCONSIN

Dr. Ziegler Joins Milwaukee Sanitarium.—Dr. Lloyd H. Ziegler, professor of neurology and psychiatry, Albany Medical College, Albany, N. Y., has been appointed associate medical director of the Milwaukee Sanitarium, Wauwatosa. Dr. Ziegler graduated in medicine from the University of Minnesota Medical School, Minneapolis, after having taken his undergraduate work and a master's degree in psychology at Indiana University. His graduate training in psychiatry and neurology was obtained at St. Elizabeth's Hospital, Washington, D. C.; the Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore, and at the Mayo Clinic, Rochester, Minn. He has been neurologist and psychiatrist in chief to the Albany Hospital in addition to his teaching position. Dr. Ziegler will lecture at the University of Illinois School of Medicine, Chicago.

GENERAL

Society News.—Dr. William C. Ryan, Philadelphia, was elected president of the International Association of Police and Fire Surgeons and Medical Directors of Civil Service Commissions at its annual meeting in Philadelphia in November. Dr. Gerald H. McMahon, Detroit, was elected vice president and Dr. Harry M. Archer, New York, secretary.

International Pediatric Congress to Be in Boston.—Dr. Henry F. Helmholz, Rochester, Minn., was elected president of the International Congress of Pediatrics, which met in Rome in September. Dr. Kenneth D. Blackfan, Boston, is general secretary, and Dr. Charles F. McKhann, Boston, is assistant secretary and treasurer. The next meeting will be held in Boston, probably in August or September 1940.

Board Examinations in San Francisco.—The American Board of Obstetrics and Gynecology will conduct its general oral, clinical and pathologic examinations for all candidates (groups A and B) in San Francisco June 13-14, immediately before the annual session of the American Medical Association. Applications for admission to the group A examinations must be filed in the secretary's office before April 1. The annual dinner for diplomates of the board will be at the Palace Hotel June 15, with Dr. William D. Cutter, secretary of the Council on Medical Education and Hospitals of the American Medical Association, as the guest speaker. For information and application blanks address the secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6).

Scientists Seek World-Wide Cooperation.—The American Association for the Advancement of Science at its meeting in Indianapolis, December 27-January 1, adopted a resolution asking the British Association for the Advancement of Science and all other scientific organizations with similar aims throughout the world "to cooperate not only in advancing the interests of science but also in promoting peace among nations and intellectual freedom in order that science may continue to advance and spread more abundantly its benefits to all mankind." In the preamble to the resolution it was pointed out that science and its applications are not only transforming the physical and mental environment of men but are adding to the complexities of their social, economic and political relations. It was also asserted that "science is wholly independent of national boundaries and races and creeds and can flourish permanently only where there is peace and intellectual freedom."

Warning Against Swindler.—A Wisconsin physician has reported that a man giving the name James Buckley recently swindled physicians, hospitals and nurses who cared for him. A physician was called to a hotel to attend the man, who said he had been under treatment at the Mayo Clinic for a year and a half for cardiovascular syphilis. Examination of his heart revealed an aortic regurgitation, and a blood test was positive for syphilis. The patient was placed in a hospital, where he remained four days under the care of a special nurse. When he left the hospital not only did he pay neither the hospital nor the nurse but he stole the nurse's watch. The man is about 5 feet 11 inches tall, weighs about 200 pounds, has dark brown hair with a little gray in it. His complexion is ruddy and three teeth are missing from the upper right side of his mouth. He gave his address as 1928 West Adams, Toledo, Ohio, and told a vague story of being employed by a firm called the Toledo Edison Company. He wore a dark brown suit and hat with a dark gray overcoat. Physicians are requested to report his whereabouts to the sheriff of Brown County, Wis., or the Green Bay Police.

Proposed Memorial to Dr. Stieglitz.—A committee of friends, alumni of the University of Chicago and members of the American Chemical Society are planning an endowment for a lectureship in honor of Julius Stieglitz, Ph.D., for many years professor of chemistry at the university and a member of the Council on Pharmacy and Chemistry of the American Medical Association. The University of Chicago and the Chicago section of the American Chemical Society are to be sponsors of the lectureship. It is planned to alternate the lectures so that they may be given one year at the university and the next at the Chicago section. Persons wishing to contribute to the fund are asked to send their donations or pledges to Benjamin B. Freud, Ph.D., treasurer, care of the Armour Institute of Technology, 3300 Federal Street, Chicago. The chairmen of the two committees in charge of the project, one representing the Chicago section of the chemical society, the other the alumni of the University, are Gustav Egloff, Ph.D., of Universal Oil Products Company and Paul N. Leech, Ph.D., of the American Medical Association. The lectureship is to be endowed in perpetuity and the funds held in trust by the University of Chicago. Dr. Stieglitz died Jan. 10, 1937.

Government Services

Children's Bureau Conference on Maternal and Infant Care

Following is the advance program for the Conference on Better Care for Mothers and Babies called by the United States Children's Bureau to meet at Washington, D. C., January 17 and 18. The meetings are being held at the Auditorium, United States National Museum, Constitution Avenue at Tenth Street N.W., except for the meeting Tuesday morning, January 18, which will be held at the White House. Representatives of the American Medical Association and of state medical societies and other medical organizations have been invited and many will attend. Information as to the proceedings of the conference will be published in THE JOURNAL as soon as available after the close of the meeting.

MONDAY, JANUARY 17

9:00 a. m. Registration.

10:00 a. m. Auditorium, United States National Museum.

KATHARINE F. LENROOT, Chief of the Children's Bureau, Presiding

Address of Welcome

The Secretary of Labor.

THE NEED TODAY

Maternal and Child Health in Relation to the Health of All the People

Thomas Parran Jr., M.D., Surgeon General, United States Public Health Service.

What is Good Care for Mothers and Babies?

Jennings Litzenberg, M.D., Professor of Obstetrics and Gynecology, University of Minnesota Medical School.

Horton Casparis, M.D., Professor of Pediatrics, Vanderbilt University School of Medicine.

What is the Need Today?

Martha M. Eliot, M.D., Assistant Chief of the Children's Bureau.

12:30 p. m. Luncheon—Members of the Conference Planning Committee.

2:00 p. m. Auditorium, United States National Museum.

WHAT IS INVOLVED IN EXTENDING GOOD CARE TO ALL MOTHERS AND BABIES

Economic Resources and Ability to Secure Good Care

Mordecai Ezekiel, Ph.D., Economic Adviser to the Secretary of Agriculture.

A. F. Hinrichs, Ph.D., Chief Economist, Bureau of Labor Statistics, United States Department of Labor.

Professional Resources and Ability to Provide Good Care

M. Edward Davis, M.D., Associate Professor of Obstetrics and Gynecology, University of Chicago School of Medicine.

Community Resources and Ability to Organize for Good Care

Felix J. Underwood, M.D., Executive Officer, Mississippi State Board of Health.

The Challenge to the Citizen

Honorable Fiorello H. LaGuardia, Mayor of New York City.

Panel to start discussion: Fred L. Adair, M.D., Hazel Corbin, R.N., George M. Lyon, M.D., C. Rufus Rorem, Ph.D., Harry S. Mustard, M.D., E. L. Bishop, M.D., Carl V. Reynolds, M.D., and others to be announced.

8:00 p. m. Meetings of Special Committees

8:15 p. m. Auditorium, United States National Museum.

FORUM DISCUSSION: HOW THE CHALLENGE MAY BE MET

MRS. J. K. PETTENGILL, *Presiding*

TUESDAY, JANUARY 18

10:00 a. m. East Room of the White House

Address

Mrs. Franklin D. Roosevelt.

SYMPOSIUM: WHAT IS BEING DONE TODAY—WHAT CAN BE DONE TOMORROW

Participants:

Martha M. Eliot, M.D., Leader.

B. F. Austin, M.D., Director, Bureau of Hygiene and Nursing, Alabama Department of Public Health.

Jessie M. Bierman, M.D., Director, Child Welfare Division, Montana State Board of Health.

Beatrice E. Tucker, M.D., Medical Director, Chicago Maternity Center, Chicago.

Philip F. Williams, M.D., Assistant Professor of Obstetrics, University of Pennsylvania School of Medicine.

Others to be announced.

Address: *The Goal We Seek*

Josephine Roche.

2:30 p. m. Auditorium, United States National Museum.

Summary of conference proceedings—Katharine F. Lenroot.

Reports of special committees.

Conclusions of the conference.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 18, 1937.

Association Opposes Notification of Abortion

A committee has been appointed by the Ministry of Health to inquire into the prevalence of abortion and the working of the law relating to it and to consider what steps can be taken by more effective enforcement of the law or otherwise to reduce the maternal mortality and morbidity from this cause. The proposal was made that abortion should be notifiable, but the council of the British Medical Association is strongly opposed to this, for it would impose on physicians a legal requirement to disclose information obtained in the course of a professional consultation and result in the patient's becoming liable to criminal proceedings. This would deter many patients from seeking the early medical aid they need. When patients take medical advice there would be imposed on the physician an obligation which would be destructive of the mutual confidence essential to the proper relationship of physician and patient. An improper burden would be imposed on the medical profession.

The council also cannot see how notification would lead to any reduction in the mortality of procured abortion. On being called to such a case the physician takes such action as is necessary for restoration of the woman's health. In this sphere notification would only discourage the patient from taking medical advice. It is argued that compulsory notification would provide additional information on the incidence of abortion. But the majority of confinements are attended by midwives, who are already required to notify abortions to the local authority by calling in a physician on the prescribed form. The proposal is fraught with considerable practical difficulty. In many cases abortion does not produce symptoms considered sufficient to necessitate medical advice, though it might prevent later complications. In cases of unlawful intervention, medical advice would be sought only on the supervention of untoward symptoms. In both groups the effect of notification would be to reduce the number of cases in which medical advice is sought. Patients are reluctant to reveal the facts even to their confidential medical advisers, and the intrusion of third parties for the purpose of investigation would be detrimental to the patient's welfare. Any advantages resulting from the procedure would be outweighed by the disadvantages.

Precautions Against Air Raids

In moving the second reading of the Air-Raid Precautions Bill Viscount Swinton, secretary of state for air, said that early in 1936 a school for instructors was established by the Air Raids Department and that it had steadily turned out 120 trained instructors a month, who had already trained something like 200,000 volunteers. In addition, every policeman had been given antigas training. Further, a special system of training for physicians had been adopted. Sixteen physicians from different parts of the country were first given special training in the treatment of gas cases. They in turn passed through the special course 10,000 physicians and the same number of nurses. The government had manufactured 20,000,000 gas masks for the use of civilians and we were the only country in the world that had devised a system of mass production. Arrangements had been made for establishing central stores for these masks, each holding 3,000,000. From them the masks would pass out in time of need to all areas of the country. The whole of the work of finding the best methods of gas proofing buildings had been done. Experiments with incendiary bombs were the foundation of a special fire fighting equipment which the government would provide. Against explosive bombs, shelters would be provided. It was estimated that the expenditure on air civilian defense would be $100,000,000 spread over three or four years, of which the state would supply 70 per cent and the local authorities the rest. The determination of this country to be strong and adequate in defense, whether active or passive, was equaled only by our earnest will to have peace.

A scheme for the protection from air raids of the members and staff of the houses of Parliament has been worked out. It comprises refuge accommodation, a plan of gas proofing and a supply of sandbags. The fire fighting arrangements will be strengthened. A stock of gas masks will be kept on the premises, and squads for rescue, clearance and decontamination will be raised from the industrial staff.

The Want of Coordination of Medical Services

The typhoid epidemic at Croydon (described in a previous letter) has aroused so much concern in London that the government has ordered an independent investigation, which is presided over by a well known lawyer, assisted by Sir Humphrey Rolleston as medical referee. The epidemic has led to a long letter in the *Times* from Lord Dawson, president of the Royal College of Physicians, and Sir Kaye Le Fleming, chairman of the council of the British Medical Association. They draw attention to a defect in our medical administration —the want of coordination between health officers and private and hospital physicians. There are now two groups of physicians: a smaller group running enlarging municipal services and a larger group who practice in the hospitals and homes of the community, and between these is an ever widening gap. Moreover, there are now two groups of hospitals—voluntary and municipal—duplicating and even conflicting, without the machinery for coordinating their activities. Our medical services have been allowed to grow up in a haphazard way in the usual English way, and coordination and systematization will come only when it is forced on us.

PARIS

(From Our Regular Correspondent)

Dec. 18, 1937.

Too Many Congresses, or Abuse of Legitimate Medical Publicity

This is the title of a timely editorial in the Nov. 17, 1937, *Concours médical*. There has been a deluge of papers during recent years, so that the task of those who attempt to index them is not an enviable one. A large proportion of these communications are presented at various congresses, and there was a surfeit of them during the exposition last summer. Many of the papers, the editorial by Dr. Noir states, are based on hasty observations and uncontrolled experiments which threaten to displace other more scientifically accurate papers in our journals. At the last Hepatic Insufficiency Congress held at Vichy, last September, there was an attendance of 2,000 and a proportionately large number of papers. There were eleven sections in the recent International Public Health Congress, and the number of papers read in each section would be adequate for an ordinary congress. Many papers have only one object in view, according to the editorial, and that is to secure publicity; hence those who have no such "urge" to see their names in print are advised to reserve their papers for the regular medical society meetings, where they can be freely discussed by those who are competent to judge their real merit. A movement ought to be initiated to limit the number of congresses by international agreement and only those should be allowed which have received the approval of the leading medical organization of the respective countries.

A fact which Dr. Noir does not mention and which is very apparent to visitors from England and the United States is a

custom that is prevalent in annual medical meetings in continental Europe. There is a tradition that the number of papers which a participant can read is unlimited, so that the program is top heavy, often twenty or thirty papers constituting an afternoon's program, in addition, here in France, to the reading of reports by some one appointed at the preceding congress, which is nothing else than a review of the literature of the particular subject. Instead of discussion being limited to five minutes and a single discussion of a paper by an individual member, there is neither time limit nor restriction of the number of times a member can take part in the discussion. It is only recently that the Académie de médecine has recommended that every paper should contain a summary. At certain local societies here, such as the Académie des sciences and the Société de biologie, only abstracts can be presented.

Latin Race Eugenics Society

An organization composed of Latin race countries interested in eugenics held its first meeting in Paris, Aug. 1-3, 1937. The countries represented included Brazil, France, Italy, Mexico, Portugal and Rumania. The questions for general discussion were mixture of races and immigration, comparative value of quantitative and qualitative increase in population, effect on a country of disproportionate increase in different classes of its population, diseases of germinal plasma and their elimination, constitutional and eugenic type and influence of age of the parents, and number of births and their sequence on the characters of the children. Some of the papers on the last three of these subjects are of special interest.

Turpin and his co-workers studied 104 cases of mongolism and found that the physical characteristics represent the sum of the anomalies that can be found in either isolated or grouped form among many of the direct or collateral relatives of the patients. Certain of these dystrophies are hereditary. They do not believe that such cases can be explained as due to infection or trauma, such as compression of the fetus, for they conform better to the germinal theory, which tends to ascribe a genetic basis to every morphogenic process. It rarely happens that those presenting the clinical picture of mongolism reach adult age and can procreate. There is usually one case in a family, the age of the mother and heredity playing an important part.

Vignes called attention to the influence of alcoholism in parents on their children. It is responsible not only for the occurrence of monstrosities but also for a large percentage of nervous and mental conditions. The statistics of Grenier were quoted, showing that if only one of the parents is a chronic alcoholic addict, dipsomania will be found in 52 per cent and, if both are heavy drinkers, in 84 per cent of the children. Pearson in 1911 said that alcoholism is a mental condition and that if the children become dipsomaniacs it is because they inherit the mental defect rather than that they are hereditarily alcoholic.

Roussy and Huguenin spoke on the role of heredity in human cancer. Experimental work during recent years appears to lend support to the existence of a hereditary predisposition to cancer, the most important contribution being that of Maud Slye, which has been confirmed by one of the investigators at the Paris Radium Institute. The observations of Roussy and Huguenin at the Cancer Institute in clinical cases do not appear to show any hereditary influence except in relatively few cases. The notion of the role of heredity in human cancer is based on cases which are difficult to interpret.

Among the papers on constitutional type and eugenics, one by Heuyer and Courthial was of interest. The subject of their paper was psychopathic constitutions in relation to eugenics. There are two opposite conceptions of the influence of heredity on psychiatric conditions. The psychiatrists believe in the existence of clear-cut hereditary morbid constitutions which are not modified during the life of the individual. They give rise by their pathologic exaggeration to well defined psychoses. Heredity is the dominant factor, the influence of environment being of no importance.

The opposing view is based on psychoanalysis, and the supporters of this view maintain that environment and not heredity is of the greater importance. Heuyer and Courthial said that neither of these theories corresponds to clinical observations. One cannot admit that heredity has the greatest influence on the formation of character of a child. The character forms at a certain period of life independently of environmental influences except in cases in which a chronic intoxication or severe injury exerts a modifying influence. These authors have suggested a "theory of tendencies" which exist in every child and are all hereditary. These tendencies are strong or feeble, and until the age of adolescence the influence of the environment can accentuate the "strong tendency," which develops into a veritable morbid constitution of the character. After adolescence there is no further evolution, the character being definitely formed, and it is only at this period that one can speak of a constitution. The first duty of the educator is to ascertain the individual tendencies of the child; when some appear that do not exist in the parents, one must always keep in mind some more remote hereditary influence such as hereditary syphilis or alcoholism.

Weill-Hallé and Meyer reported the results of a survey of 160 families of less than five children and of eighty-four above this number, in order to determine the longevity of the children in large families. In grouping those with from five to seven children, a mortality of 15 per cent was noted, rising to 18 per cent in those having eight or more children. Large families are a rarity among those having a steady or large income in Paris, whereas the opposite is true of the laboring classes. The majority of deaths in large families is the result of inadequate medicosocial surveillance.

Honorary Professors

The minister of national education has recently conferred the title of Honorary Professor on three distinguished members of the Faculty of the Paris Medical School: Roussy who was elected rector of the University of Paris; Brindeau, obstetrician, and Sergent, phthisiologist. The last two have reached the age limit.

BERLIN

(From Our Regular Correspondent)

Nov. 29, 1937.

New Law for Regulation of the Medical Profession

The national führer of physicians has just proclaimed an immediately effective "Law for Regulation of German Physicians," which supersedes previous legislation of the kind and seeks to regulate every aspect of the doctor's professional life. It contains many noteworthy stipulations and provisions. The body of the statute is preceded by a preamble in which the moral obligations of the physician are defined: He is required to serve the health of the individual citizen and of the nation. Moreover, it is the duty of the medical profession as a group to preserve and promote the nation's health, sound heredity and racial purity. The public duties of the medical man have already been set forth in the national statute of physicians. The medical profession is not a trade (this statement is of great significance, as it represents the answer to a long standing demand of the profession for some official pronouncement on this point). To quote further from the preamble: "No piece of legislation can cover all the duties of the profession's members. The doctor who would properly discharge his obligations to society and to his colleagues must think of himself as a public servant."

This new, meticulously prepared ordinance reflects the spirit of the new régime both in its cadre and in its content.

The first main division treats of general professional precepts. Professional secrecy is significantly discussed: in addition to those exceptional circumstances which have heretofore absolved the doctor from this obligation, the revelation of professional secrets is now regarded as not unethical if made "in the fulfilment of a legitimate, moral duty in the interests of any objective that is felt to be socially desirable or if a menace to public welfare is the predominant consideration." If a question arises as to the ethics of such a disclosure the doctor must carefully weigh the various factors pro and con, but the public welfare should receive the benefit of any doubt. Accordingly the inviolability of an individual patient's confidences is no longer conceived as a more or less absolute professional obligation. In dubious cases the public good now definitely takes precedence over that of the patient. This new doctrine will facilitate the solution of age-old forensic problems such as that which confronts the doctor who treats a fugitive from justice and who thus becomes inadvertently the repository of guilty knowledge. A doctor's helpers, namely, nurses and so on, are likewise supposed to maintain secrecy with respect to the patients.

The physician should make every effort to combat whatever is inimical to national strength and fecundity. He should encourage the desire to procreate and in the course of his professional activities he shall discourage contraceptive measures in the absence of any legitimate grounds therefor. No interruptions of pregnancy or sterilization operations may be performed unless all legal stipulations have been satisfied.

The doctor is obliged to improve himself professionally by graduate study. He should cast aside any prejudice in favor of or against a particular trend in medicine and make himself conversant with all significant therapeutic methods. In each case of illness that he is called on to manage he should always seek the shortest route to the optimal end result. The foregoing clause is an indirect reference to the methods of nature medicine and kindred movements which, as so often mentioned in these letters, have acquired great importance in present-day Germany. Graduate medical study has for some time been regulated by law and a system of compulsory attendance on graduate courses has been in force (THE JOURNAL, Nov. 9, 1935).

Maintenance of office hours at more than one location requires a special permit. If one general practitioner maintains an office at a certain address, no other general practitioner may open an office in the same building. This holds true also for specialists in the same or in kindred disciplines. If a doctor moves away from a certain neighborhood, no other doctor can establish a practice there until six months has elapsed without the express permission of the first doctor or of the local medical organization. The local groups can, if public health considerations so demand, require that general practitioners, gynecologists and surgeons maintain both office and residence at the same address. Special permits are required for seasonal changes in the place of practice (by spa physicians, for example). No doctor should extend his practice (namely, make sick calls) beyond a circumscribed territory allotted him unless it should be a question of some area served by no other practitioners.

It is illegal for a doctor to manage a case solely by correspondence, telephone or any type of absent treatment. A doctor is forbidden to go about practicing medicine now in this place and now in that; he must maintain a permanent location. Another new provision is that a physician is now required to keep for five years at least a record of all the important clinical data accumulated in the course of his practice and of all therapeutic methods used by him. These records are amenable to the clauses regarding professional secrecy.

Great care should be exercised in the matter of expert certification and legal testimony. A doctor is forbidden to issue any so-called courtesy certificates. Professional opinion relative to the equity of a physician's honorarium may not be introduced in court excepting on special orders from the national chamber of physicians. Other activities requiring special authorization are the conducting of so-called medical question boxes (such as appear in the newspapers) and the editing or co-authorship of so-called doctor-books, those manuals which encourage self treatment by the public.

No doctor may undertake the unauthorized instruction of the nursing personnel or hold any unauthorized examination of a nurse's skill or knowledge. The amount of a physician's fee is still governed by the current statute of medical honorariums. The maximal charges under this statute cannot be exceeded without special authorization or the existence of a written contract between physician and patient. A practitioner is not required to ask any remuneration for his services to indigent persons, relatives, intimate friends and colleagues and their dependents. But in all other cases he must not ask less than the legal minimum. Liquidation of honorariums due should as a rule take place at least once in four years.

A doctor should manifest for his colleagues the same respect and consideration that he expects for himself; unwarranted disparagement of the professional knowledge or the therapeutic methods of a fellow physician is highly unethical. If a doctor enters a case that has already been treated by another practitioner, he may make house visits to the patient only after he has been assured that the patient has foregone the further services of the first physician; if the patient has not informed the first doctor of the situation, the second doctor must do so himself. If a doctor is called to treat another doctor's patient in an emergency, he should immediately endeavor to do whatever the attending practitioner would wish done and then leave all subsequent treatment to the latter. If more than one doctor is called in an emergency, the first man to arrive on the scene should, in the absence of any other agreement, undertake the treatment. On the other hand the doctor may, during office hours, treat whoever comes to him with no restriction.

If one doctor is called into consultation by another, he should not refuse in the absence of some good reason. Nor should requests by the patient for the calling in of a consultant ever be refused. If a patient is referred from another doctor for treatment, the second doctor shall turn the patient over to the attending physician on the latter's request, even if the second doctor believes further treatment necessary. Agreements between doctors with regard to reciprocal substitution should be the rule. Patients taken over by a locum tenens must be relinquished to the original practitioner. The practice of a deceased physician may be carried on by substitute for a period of three months or perhaps longer for the benefit of the widow and children; such an arrangement must be authorized by the local medical organization. The locum tenens and the assistant of a still active practitioner cannot settle within the area of this doctor's practice within less than one year after termination of their association with him unless he approves of such a move. A health service doctor must abstain from treatment of the persons observed by him excepting in emergencies and must in no way alienate these patients from their own family practitioners.

Spa physicians must give up their outside patients after the course of treatment, the kur, has ended. No outside practitioner may draw up a plan of therapy for a patient recommended to a watering place; the medical staff of the resort must be free to introduce whatever measures it deems indicated. A doctor who visits a spa for the benefit of his own health is forbidden to practice his profession there.

It is illegal for a doctor to receive compensation, monetary or otherwise, in return for recommending to his patients another doctor or an institution.

The establishment of a joint practice or medical partnership is forbidden. If such an arrangement already exists it may continue only by special permission of the chamber of physicians. Joint ownership of the more elaborate medical equipment, such as x-ray apparatus, also requires a special permit.

Commercial advertising and soliciting in any way connected with medical practice is forbidden to physicians; specifically no discussion of therapeutic substances and appliances in which a doctor is commercially interested must enter into his publications, lectures, radio talks and so on. Records of cases and operations are not to be discussed in print elsewhere than in the medical journals. It is illegal to advertise concerning office hours for free medical advice or concerning advice and treatment by correspondence. No doctor should treat a patient in collaboration with a lay practitioner or in any way become a party to treatment by a layman. He must never allow a lay person to perform any of his own proper duties nor may he act as strawman for lay practitioners. Disinterested lay persons are not to be permitted to witness operations, hypnoses and so on. A physician must not request or authorize the publication in newspapers or elsewhere of any testimonial or expression of gratitude relative to his professional activities. The acceptance of office in a public health organization under lay auspices is contingent on official approval. Doctors are expected to collaborate in the campaign against fraudulent therapeutic procedures, substances and appliances. A doctor must obtain a special permit if he wishes to obtain the rights of commercial exploitation of pharmaceutic innovations. This permit will be revoked at any time if it is found that the doctor's commercial activities conflict with his professional duties. All contracts relative to the mentioned enterprises are subject to official approval. It is illegal for a doctor to use his professional title for commercial purposes, as in the title of a firm or on the label of a pharmaceutic product. This prohibition would apply, for example, to a label inscribed "——— Remedy, prepared according to Professor X's formula." Commercial connections that become outlawed by the new legislation must be dissolved at once without exception. No doctor may request or receive any gift or favor in exchange for his prescription or recommendation of a certain drug. Only a reasonable number of pharmaceutic trade samples should be requested or used; the physician must never offer these samples for sale. No doctor may request or receive any more than a defrayal of expenses involved for the tests of and reports on a pharmaceutic substance, nor may he receive additional compensation in any form whatever for such services. The enforcement of this clause will be supervised directly by the national chamber of physicians. A doctor will allow the publication of his expert report only after he has satisfied the national chamber that he has received no extralegal remuneration. A doctor cannot allow his professional opinion or testimonial to be used by laymen for commercial purposes. For discussion and reports in which a physician recommends a particular pharmaceutic product, the author may receive no remuneration in excess of the customary honorariums paid by the journal to its contributors. In writing for publication, a doctor should be guided solely by his scientific convictions.

A doctor must not bestow favors of any sort or hold out a prospect of favors for the purpose of obtaining some professional advantage.

The proper designations of specialists are once more considered; these remain substantially as described in THE JOURNAL July 27, 1935, page 294. The specific educational requirements for candidates in the specialties are basically the same with certain additions. Gynecologists must now have completed a two year course in obstetrics. Neurologists and psychiatrists must have devoted one year to the study of neurology and another year to the study of psychiatry. In general, about one year of additional study has been added to the prerequisites for admission to all the specialties. This means an extra year of training in the discipline of choice. Each prospective specialist must now complete one year of training in general practice or internal medicine and, conversely, a prospective internist must complete a year's training in general practice, surgery or gynecology. The foregoing requirements afford the specialist first hand experience of a wide variety of clinical material outside his own particular discipline and he thus will be thoroughly grounded in the entire field of medical science. No important qualitative changes have been made in the type of training required of the candidate for a medical specialty. A doctor no longer becomes a specialist merely on the basis of a special examination. The specializing physician is now as a matter of fundamental principle excluded from general practice; he must virtually limit his activities to his own particular discipline and never permit his work to develop into a general family practice.

The next principal section of the new statute deals with public advertising by independent practitioners. Public notice of the opening of an independent practice at a certain location must contain no more than the doctor's name, office address and the same title that he is authorized to display on his nameplate. The advertisement can appear in only three editions of any one newspaper. A similar announcement may be run in the newspapers (but only in one edition of the same paper) before or after an absence of more than a fortnight on the part of the doctor or if the doctor is resuming practice after a prolonged illness. The national chamber of physicians exercises direct supervision of these public advertisements. The form and size of the advertisement are regulated by local custom. Information with respect to establishment of practice, absence or illness must be made public solely by means of the mentioned announcements in the press.

The nameplates displayed by physicians are subject to drastic regulation. In general only the following information may appear on the sign: doctor's name, academic title (Dr. med. and so on), official designation as general practitioner or specialist, office hours, telephone number. Certain additional styles are permitted: "Obstetrician" for a general practitioner who is available for confinement cases; "Nature Medicine Practice" for a doctor who utilizes the procedures of nature medicine. Special permits, granted only if all legal requirements are satisfied, are necessary for references to homeopathy or tropical diseases. Then too the office may be legally designated "Roentgen Institute" or "Medical Diagnostic Institute." Finally, doctors specially licensed to administer serologic tests may describe themselves as "officially licensed for serologic blood examinations." The sign must not be fashioned or displayed in a way that may become obtrusive; its dimensions must not exceed 35 by 50 cm. Only in exceptional circumstances may more than one sign be displayed at the same address. The foregoing regulations likewise apply to the headings of a practitioner's letter paper, prescription blanks and so on. Members of hospital staffs are permitted to display printed references to their institutional activity on letter and prescription paper but not on their office signs. The official title "spa physician" will be discontinued in future.

The foregoing comprise the most interesting and significant provisions of the new legislation.

At the same time new stipulations have been decreed relative to the retirement from and acquisition of a medical practice. A doctor who relinquishes his practice may accept from his successor indemnification solely for real or personal property involved in the transfer. In exceptional instances the local medical organization may authorize the payment of a special indemnity to a deceased practitioner's surviving dependents if the latter have been left in bad economic circumstances and if the late doctor's practice had been his life's work.

ITALY

(From Our Regular Correspondent)

Dec. 4, 1937.

Experimental Vaccination Against Tuberculosis

Dr. Alberto Ascoli, in a recent lecture, reported results of studies on the preventive value of antituberculosis vaccines prepared with living or killed tubercle bacilli. The studies were carried on from 1932 to 1934 at the laboratorio di patologia comparata of the Milan University and at the istituto vaccinogeno antitubercolare of Milan. The experiments were performed on ninety-four calves, which were placed in two different groups. One group received the vaccines subcutaneously and the other intravenously. Each group consisted of four lots of animals, which were given doses of from 40 to 150 mg. prepared from living bovine tubercle bacilli, or from 50 to 500 mg. prepared from killed bovine or human tubercle bacilli. The organic defense induced by the vaccines was tested by inoculating the animals with several doses of virulent bovine tubercle bacilli or by placing them in contact with animals that had open pulmonary tuberculosis. The animals that were administered vaccines prepared with living tubercle bacilli and later on inoculated with virulent bovine tubercle bacilli did not develop specific lesions. Those given the vaccines prepared with killed tubercle bacilli and then placed among animals that had open tuberculosis were all contaminated with the disease.

Treatment of Pleurisy

The Federazione per la lotta contra la tubercolosi met recently, and Professor Fici of Palermo spoke on the modern trends in the treatment of parapneumothorax pleurisy. According to the speaker it is advisable to resort to thoracentesis as soon as the acute phase of pleuritis passes, especially if one believes that there is empyema. Pleural lavages are indicated besides thoracentesis when there is a tendency to chronic pleuritis and also when the exudates show, by cytologic study, a prevalence of granulocytes over lymphocytes.

Professor Beninato spoke on the surgical treatment of serofibrinous pleurisy and simple tuberculous empyema. He performed pneumothoracentesis after appearance of the acute symptoms and before formation of large amounts of exudates. In cases of serofibrinous pleurisy the operation is followed by frequent pleural lavages, which are done with solutions containing detergent substances or substances that dissolve fibrins. The solutions are used alternately by doing a series of lavages with three lavages of each substance in solution. The speaker's patients recovered by this method in 75 per cent of the cases, there was transformation in empyema in 15 per cent and the exudates were not modified in 10 per cent. Pneumothoracentesis, when not followed by lavages, gives less satisfactory results. In simple empyema the best results are obtained by lavage. By this method the speaker's patients recovered in 53 per cent of the cases.

BUCHAREST

(From Our Regular Correspondent)

Nov. 7, 1937.

Decrease in Importation of German Drugs

According to *Pharmacia,* a Bucharest journal, the custom authorities, when compiling the statistics of imports of drugs and fine chemicals for recent years, established that there has been a decrease of about 30 per cent in the importation of German preparations. The surprising loss of the Rumanian market for German goods is partly the outcome of the boycott of German goods by Jewish importers and partly the result of less activity of the representatives of German pharmaceutical manufacturers. No less contributory has been the great activity of Rumanian pharmaceutical manufacturers. The restrictions on importation and the great difficulty of exporting foreign currency have been conducive to the development of Rumanian production to such an extent that with the exception of fine chemicals a considerable part of the home demand can be supplied by Rumania.

Professor Marinescu Lectures in Paris

Dr. Marinescu, professor of neurology and psychiatry at the University of Bucharest, was invited by the French government to lecture before the congresses held at the Paris exposition. Marinescu was pleased to accept this invitation and lectured before the medicopsychologic society July 25 on hysteria. Next day at the meeting of the Infantile Psychiatric Congress he read a paper which he prepared in collaboration with Jonescu-Sisesti, professor, and Kraindler, lecturer at the university of Bucharest. On the same day he accepted an invitation to read a paper at the Biotypologic Congress on the human constitution. July 28 at the Psychologic Congress at the Sorbonne under the presidency of Pierre Janet he read a paper, prepared in collaboration with professor Jonescu-Sisesti and Coppelmann. August 1 at the Congress on Eugenics and Heredity he read a paper on acromegaly and gigantism, prepared in collaboration with Jonescu-Sisesti and Alexanin-Buttu. The vigor of this aged man was the subject of general admiration.

Prize for Best Work on Schizophrenia

A prominent professor of the Bucharest university, who recently retired from his position, deposited 800,000 lei ($6,000) on behalf of the Medical Academy with the understanding that the interest of this sum every three years, 72,000 lei ($540), shall be awarded to the author of the best work written during the past three years on the treatment of schizophrenia. Only such works shall be considered as show an undoubted, real advancement. The reward will bear the name of Professor Ioan Nanu-Muscel.

Revista de Pediatrie si Puericultura

A new medical periodical, the *Revista de Pediatrie si Puericultura,* is edited by Prof. Gheorghe Popoviciu, director of the pediatric clinic in Cluj. Popoviciu used to be the collaborator of Paul György, then professor of pediatrics at the University of Heidelberg, Germany, at present in Cleveland, with whom he wrote many papers. The new periodical will appear monthly, for the time being, and later on bimonthly. The publishers of the paper are the Societate de Pediatrie si Puericultura, in Cluj, capital city of Transylvania, and the editorial office is at the Pediatric Clinic, Cluj University.

Marriages

HART E. VAN RIPER, Madison, Wis., to Miss Mary Virginia Smith of Washington, D. C., Oct. 14, 1937.

DAVID E. W. WENSTRAND, Milwaukee, to Miss Margaret Letchworth of Minneapolis, Oct. 9, 1937.

OSCAR WILLIAM HURTH, Cedarburg, Wis., to Miss Mary Ellen Kolls of Milwaukee, Oct. 19, 1937.

HERBERT J. SCHWARTZ, Ontario, Ore., to Miss Alberta Wahl at Clarkstone, Wash., Oct. 14, 1937.

HAROLD HORN LOWENSTEIN, Brooklyn, to Miss Lysette Teven of New York, Nov. 21, 1937.

CLARENCE E. ZENNER of Cadott, Wis., to Miss Lorraine Huston of Milwaukee, Oct. 9, 1937.

RALPH H. HIGHMILLER, Olympia, Wash., to Miss Alice Long in Seattle, Sept. 18, 1937.

WILLIAM J. KLEIS to Miss Marion Design, both of Milwaukee, Oct. 13, 1937.

ROBERT E. WINN to Miss Elizabeth Smith, both of Dallas, Texas, Nov. 5, 1937.

CARL B. POPE to Miss Helen Hyde, both of Milwaukee, Oct. 16, 1937.

Deaths

Emmet Rixford ✠ San Francisco; Cooper Medical College, San Francisco, 1891; professor of surgery, emeritus, Stanford University School of Medicine, where he was professor of surgery from 1909 until 1930; formerly adjunct professor of surgery and later professor of surgery at his alma mater; instructor in surgery, Training School for Military Officers, U. S. Army, from March to December, 1918; fellow and past president of the American Surgical Association; member and past president of the Pacific Coast Surgical Association; member of the Society of Clinical Surgery, California Academy of Medicine, California Academy of Science and the Société Internationale de Chirurgie; fellow of the American College of Surgeons; consulting surgeon to the Lane and San Francisco hospitals; aged 72; died, January 2, in the Peter Bent Brigham Hospital, Boston.

John Randolph Haynes ✠ Los Angeles; University of Pennsylvania Department of Medicine, Philadelphia, 1874; formerly associate professor of gynecology at the University of Southern California School of Medicine; president of the board of water and power commissioners; at various times member of the city civil service commission, the California State Board of Charities and Correction, the Los Angeles County Public Welfare Commission and other civic bodies, and the State Council of Defense during the World War; since 1923 regent to the University of California; aged 84; died, Oct. 30, 1937, in the Hospital of the Good Samaritan, of cerebral hemorrhage.

Edward Sparhawk Hatch ✠ New Orleans; Harvard University Medical School, Boston, 1899; member of the American Orthopedic Association and the American Academy of Orthopedic Surgeons; member and past president of the Clinical Orthopedic Society; fellow of the American College of Surgeons; professor of orthopedics, Tulane University Graduate School of Medicine; served during the World War; aged 62; consulting orthopedic surgeon to the New Orleans Hospital and Dispensary for Women and Children and the United States Public Health Service; chief orthopedic surgeon to the Touro Infirmary, where he died, Oct. 20, 1937, of cerebral hemorrhage.

David Durward Hogan ✠ Lieut. Colonel, M.C., U. S. Army, Fort Des Moines, Iowa; Rush Medical College, Chicago, 1896; veteran of the Spanish-American War; entered the medical corps of the regular army as a first lieutenant in 1915; was promoted to captain in 1917 and in 1935 to lieutenant colonel; aged 63; died, Oct. 16, 1937, in the Army and Navy General Hospital, Hot Springs National Park, Ark., of acute coronary occlusion.

George Francis Keenan ✠ Boston; Tufts College Medical School, Boston, 1906; member of the New England Obstetrical and Gynecological Society; fellow of the American College of Surgeons; served during the Spanish-American and World wars; aged 58; on the staffs of the Whidden Memorial Hospital, Everett, Mass., Community Hospital, Winthrop, and St. Elizabeth's Hospital, where he died, Oct. 26, 1937, of pneumonia.

William Hunter Workman, Newton, Mass.; Harvard University Medical School, Boston, 1873; member of the Massachusetts Medical Society; made numerous expeditions in Ceylon, Java, India and the Himalayan mountains for the purpose of studying the people, their art and architecture; wrote various books on his exploits; aged 90; died, Oct. 7, 1937, of coronary disease.

Edward Lee Meierhof ✠ New York; University of Maryland School of Medicine, Baltimore, 1881; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; formerly on the staffs of the Sydenham Hospital and the New York Eye and Ear Infirmary; aged 76; died, Oct. 25, 1937, of carcinoma.

Everett Flood, Friendship, Maine; Medical School of Maine, Portland, 1881; member of the Massachusetts Medical Society; past president of the Boston Society of Psychiatry and Neurology; for many years superintendent of the Monson State Hospital, Palmer, Mass.; aged 82; died, Oct. 16, 1937, of chronic interstitial nephritis.

Francis J. Hackney, Chattanooga, Tenn.; University of the South Medical Department, Sewanee, 1899; member of the Tennessee State Medical Association and the American Academy of Ophthalmology and Oto-Laryngology; owner of the Hackney Eye, Ear, Nose and Throat Hospital; aged 64; died, Oct. 28, 1937.

Willard Phelps Earngey, San Marcos, Texas; Hahnemann Medical College and Hospital, Chicago, 1915; member of the Associated Anesthetists of the United States and Canada; served during the World War; formerly county physician in Winnebago County, Ill.; aged 48; died, Oct. 28, 1937, of myocarditis.

George Silas Drake Jr. ✠ St. Louis; Johns Hopkins University School of Medicine, Baltimore, 1901; served during the World War; on the staffs of the Barnard Free Skin and Cancer Hospital and St. Luke's Hospital; aged 62; died, Oct. 28, 1937, in the Peter Bent Brigham Hospital, Boston.

Oscar Nicholas Mortensen, Wisconsin Rapids, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; fellow of the American College of Surgeons; on the staff of the Riverview Hospital; aged 51; died, Oct. 24, 1937, of myocarditis.

Fred Andrew Johnson ✠ Greenville, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; formerly bank president, member of the school board and city health officer; aged 61; died, Oct. 22, 1937, in Chelsea, of heart disease.

James E. Helms, Louisville, Ky.; Joplin (Mo.) Medical College, 1881; Louisville Medical College, 1895; member of the Kentucky State Medical Association; aged 82; died, Oct. 22, 1937, of bronchial pneumonia and cardiovascular disease.

Roy Ellsworth Hall, Portland, Ore.; John A. Creighton Medical College, Omaha, 1914; member of the Oregon State Medical Society; served during the World War; aged 51; died, Oct. 13, 1937, of hypertension and chronic nephritis.

John Wesley Faust ✠ Kansas City, Kan.; Cornell University Medical College, New York, 1903; past president of the Wyandotte County Medical Society; aged 60; died, Oct. 29, 1937; of coronary occlusion and arteriosclerosis.

Jesse Newman Reeve, Washington, D. C.; Georgetown University School of Medicine, Washington, 1893; aged 71; died, Oct. 25, 1937, in the Georgetown Hospital, of fatty degeneration of the liver, with terminal septicemia.

James Dixon Collier, Powell Station, Tenn.; Cincinnati College of Medicine and Surgery, 1882; University of Nashville (Tenn.) Medical Department, 1882; chairman of the county high school board; aged 83; died, Oct. 23, 1937.

Gordon Lawrence McLellan, San Leandro, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1913; aged 48; died, Oct. 28, 1937, of a self-inflicted knife wound of the throat.

Edwin William Link ✠ Palestine, Texas; Bellevue Hospital Medical College, New York, 1883; past president of the Anderson County Medical Society; member of the school board; aged 79; died, Oct. 24, 1937, of cancer.

Willard Pierrepont Millspaugh ✠ Los Angeles; Columbia University College of Physicians and Surgeons, New York, 1900; on the staff of the Hospital of the Good Samaritan; aged 65; died, Oct. 28, 1937, of coronary occlusion.

Charles Edward Thompson Jr., ✠ Scranton, Pa.; Columbia University College of Physicians and Surgeons, New York, 1923; medical superintendent of the Scranton Private Hospital; aged 38; died, Oct. 17, 1937.

Samuel Hammill Snider, Detroit; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1881; aged 80; died, Oct. 31, 1937, in the Epworth Hospital, South Bend, Ind., of carcinoma of the colon.

Samuel De Nosaquo ✠ Milwaukee; Marquette University School of Medicine, Milwaukee, 1913; on the staff of the Mount Sinai Hospital; aged 58; was found dead, Oct. 28, 1937, of coronary sclerosis.

William Gaston ✠ Clarksburg, W. Va.; Eclectic Medical Institute, Cincinnati, 1884; an Affiliate Fellow of the American Medical Association; aged 78; died, Oct. 19, 1937, of cardiovascular disease.

Robert Hickman Burney, Oakland, Calif.; University Medical College of Kansas City, Mo., 1901; aged 69; died, Oct. 11, 1937, in Agnews, of chronic myocarditis and cerebral arteriosclerosis.

Monroe D. Lehr, Lykens, Pa.; Jefferson Medical College of Philadelphia, 1884; member of the Medical Society of the State of Pennsylvania; aged 77; died, Oct. 12, 1937, of cerebral hemorrhage.

Goff MacKinnon ✠ Seattle; University of Pennsylvania School of Medicine, Philadelphia, 1916; on the staff of the Swedish Hospital; aged 47; died, Oct. 31, 1937, of coronary thrombosis.

James M. Hubbard, Mountain Grove, Mo.; Louisville (Ky.) Medical College, 1893; member of the Missouri State Medical Association; aged 84; died, Oct. 25, 1937, of bronchopneumonia.

Arthur F. Lyon-Campbell, Milwaukee; Milwaukee Medical College, 1898; served during the World War; aged 67; died, Oct. 27, 1937, of carcinoma of the lungs and arthritis deformans.

William Henry Morrow, Cotulla, Texas; St. Louis College of Physicians and Surgeons, 1893; served during the World War; aged 67; died, Oct. 18, 1937, in San Antonio, of uremia.

George Oliver Remy, Ainsworth, Neb.; Medical College of Ohio, Cincinnati, 1877; member of the Nebraska State Medical Association; aged 86; died, Oct. 25, 1937, of angina pectoris.

Harry T. Gray, Alma, Mich.; Detroit College of Medicine, 1907; member of the Michigan State Medical Society; aged 54; died, Oct. 11, 1937, of a self-inflicted bullet wound.

Charles Peek Steeves, Denver; McGill University Faculty of Medicine, Montreal, Que., Canada, 1896; aged 72; died, Oct. 2, 1937, in Moncton, N. B., of mesenteric thrombosis.

Frank Fitzgerald, Morrison, Ill.; Rush Medical College, Chicago, 1886; member of the Illinois State Medical Society; aged 80; died, Oct. 24, 1937, of carcinoma of the sigmoid.

Hannah Goodridge, San Jose, Calif.; Pulte Medical College, Cincinnati, 1903; member of the California Medical Association; aged 73; died, Oct. 26, 1937, of carcinoma.

Percy Hobbs Abbott ✠ Waterboro, Maine; Medical School of Maine, Portland, 1910; aged 52; died, Oct. 10, 1937, at his summer home in Ossipee Hill, of cerebral hemorrhage.

Grover C. Hardie, Fort Pierce, Fla.; Atlanta (Ga.) School of Medicine, 1911; member of the Florida Medical Association; aged 49; died, Oct. 25, 1937, of coronary thrombosis.

William A. Sims, St. Louis; Eclectic Medical Institute, Cincinnati, 1883; aged 80; died, Oct. 27, 1937, in Los Angeles, of chronic myocarditis and cerebral hemorrhage.

Charles Wesley Treverton, Greason, Pa.; University of the City of New York Medical Department, 1886; aged 83; died, Oct. 17, 1937, of diabetes mellitus.

William Leonard Renick, Long Beach, Calif.; University of Louisville (Ky.) Medical Department, 1892; aged 67; died, Oct. 23, 1937, of coronary thrombosis.

Charles Fremont Ross, Saunemin, Ill.; Rush Medical College, Chicago, 1881; aged 80; died, Oct. 15, 1937, in Cleveland, Ohio, of cerebral hemorrhage.

Madeleine Marquette-Baker, Denver; Gross Medical College, Denver, 1888; aged 77; died, Oct. 28, 1937, of arteriosclerosis and angina pectoris.

Woodbury Pulsifer, Washington, D. C.; Columbian University Medical Department, Washington, 1897; aged 82; died, Oct. 20, 1937, of myocarditis.

Eva Wilensky Goldstein, Brooklyn; New York Medical College and Hospital for Women, 1905; aged 54; died, Oct. 15, 1937, of cerebral sclerosis.

Elmer Albertus Miller, Brooklyn; University of the City of New York Medical Department, 1886; aged 76; died, Oct. 23, 1937, of heart disease.

Robert Emmett McCarten, Butte, Mont.; Jefferson Medical College of Philadelphia, 1910; aged 53; died, Oct. 3, 1937, of heart disease.

John A. Snowden Sr., Winchester, Ky.; Louisville (Ky.) Medical College, 1879; aged 85; died, Oct. 8, 1937, at a hospital in Lexington.

James Murray Johnston, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1882; died, Oct. 23, 1937, in St. Catharines.

George King, Queen City, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1881; aged 79; died, Oct. 1, 1937, of sarcoma.

Thaddeus L. Loofbourrow, Eureka, Calif.; Rush Medical College, Chicago, 1890; aged 70; died, Oct. 20, 1937, of carcinoma.

A. Lee Smith, Crystal, Mich.; Detroit College of Medicine, 1896; aged 75; died, Oct. 21, 1937, in Alma, of cancer of the throat.

Edward A. Smith, Birmingham, Mich.; Detroit Medical College, 1885; aged 76; died, Oct. 5, 1937, of diabetes mellitus.

William James Donlon, Denver; Rush Medical College, Chicago, 1902; aged 58; died, Oct. 13, 1937, of pneumonia.

Correspondence

INFECTIOUS JAUNDICE IN HAWAII

To the Editor:—I was interested in your recent editorial concerning the importance of spirochetal jaundice in the United States (THE JOURNAL, October 2, p. 1128). Since no mention was made of this disease in Hawaii, I am submitting to you one of my recent reports on this subject. You may be interested to know that since our first finding of this disease in the territory in October 1936 there have been reported by physicians a few cases of Weil's disease from the various islands including Hawaii, Maui and Kauai.

J. E. ALICATA, PH.D., Honolulu, Hawaii.
Parasitologist, University of Hawaii.

To the Editor:—In THE JOURNAL, October 2, I read with interest your editorial on infectious jaundice.

I thought it might be well to report from Hawaii. In January 1928 a young Japanese man died of the disease in the sugar plantation hospital of which I have charge. Since then, I have had more than forty cases.

Since 1936 the diagnosis has been made from clinical symptoms alone. During 1936, a parasitologist, J. E. Alicata, Ph.D., from the United States Public Health Service, was on our island investigating trichinosis and I asked him to come out to our plantation and try to demonstrate the leptospira of infectious jaundice in a case I had at the time. He succeeded in doing so, and this was the first time the organism was demonstrated on these islands.

I wrote on the subject for our county society and since that time have been trying to do something about treatment. The injection intravenously of whole blood from a donor who has recovered from the disease apparently has a definitely favorable effect. I now have a case of a young Japanese man whose condition was extreme. My assistant, Dr. W. F. Hume, gave him 500 cc. of whole blood from the same donor as the previous case. Prompt improvement resulted and recovery is assured. These two recoveries were spectacular. I thought they might be of interest to others.

THOMAS KEAY, M.D.C.M., Pepeekeo, Hawaii.

INJECTION TREATMENT OF HERNIA

To the Editor:—I read the editorial on the injection treatment of hernia (THE JOURNAL, October 30, p. 1456) with great interest. The organization of which I am chairman has asked me to write to you voicing its approval.

There is no question that there has been a recent wave of enthusiasm over this method of treatment. But the danger in it lurks in the inexperienced accepting this as a simple office procedure, and the consequences of the indiscriminate use will result not only in failure but also in deaths. There is no doubt that the use of 16 minims of thuja was done by some inexperienced physician, as the dose is generally accepted as 2 minims.

It is for this reason that the Society for the Injection Treatment of Hernia passed a resolution of commendation for you for this timely warning, that it be used "under circumstances in which unusually careful technic and suitable care are possible." In addition we feel that only those experienced in this method should use it and that any one else who is interested should first study the entire subject carefully and receive thorough instruction in its use before attempting to treat patients by this method.

MARTIN BIEDERMAN, M.D., New York.
Chairman, Society for the Injection
Treatment of Hernia.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VITAMIN REQUIREMENTS AND PRESENCE IN FOODS

To the Editor:—What is the daily number of vitamin A units required for an adult? A patient on account of obesity and diabetes is on a daily allowance of 171 Gm. of carbohydrate, 35 Gm. of fat and 65 Gm. of protein. On such a small amount of fat is there danger that she is not getting enough units of vitamin A? How many additional units of vitamin A shall I give her and in what form of concentrate? Whole cod liver oil I cannot use, as she cannot take cod liver oil; besides, cod liver oil would increase the fat too much. What number of units of vitamin B is the daily dose? vitamin G? vitamin C? vitamin D? The government has issued a new pamphlet on vitamins, but the supply is exhausted. Is there a book which gives this information?

M.D., Missouri.

ANSWER.—In the present state of scientific knowledge only tentative estimates of daily vitamin requirements can be made. However, there is good evidence for the belief that prolonged daily intakes of less than 2,000 international units of vitamin A, 200 international units of vitamin B_1 and 300 international units of vitamin C will lead to the development of definite deficiency disease. The consensus is that optimal intakes which will support growth, promote optimal nutrition and provide for maximum storage are approximately 4,000 to 6,000 international units of vitamin A, 300 to 400 international units of vitamin B_1, 600 to 1,200 international units of vitamin C and 600 Sherman-Bourquin units of vitamin G (riboflavin). No definite requirements for vitamin D for adults can be stated. For infants the Council on Foods is of the opinion that at least 135 international units of vitamin D is required to prevent rickets, and 400 international units is required for best growth.

The diet prescribed for the patient with obesity and diabetes is estimated to supply approximately 1,260 calories, which is obviously considerably below her maintenance requirements. In such restricted diets the intake of all the vitamins is likely to be below the optimal allowance and may be below minimum requirements. Natural foods rich in vitamins should be selected as far as possible, and vitamins A and B_1 particularly probably should be supplied in concentrated form. The important natural sources of vitamin A are butter fat, green leafy vegetables, yellow vegetables and fruits, and tomatoes (either raw or canned).

There is available a variety of commercial preparations which supply vitamin A in concentrated form. The Council on Pharmacy and Chemistry has accepted a number of brands of cod liver oil concentrate dispensed either in liquid (bottled or in capsules) or in tablet form, as well as a solution of pure carotene in cottonseed oil. The cod liver oil concentrate capsules supply approximately 10,000 international units of vitamin A and 1,400 units of vitamin D per capsule. The cod liver oil concentrate tablets supply approximately 3,000 U. S. P. units of vitamin A and 300 international units of vitamin D per tablet, while the solution of carotene in oil provides not less than 7,500 units of vitamin A per gram, with no vitamin D. The Council has also accepted several brands of halibut liver oil marketed either in liquid form or in capsules which provide approximately 10,000 international units of vitamin A and 170 international units of vitamin D per capsule. Information concerning the various accepted brands may be found in N. N. R. for 1937. Concentrated sources of vitamin B_1 are dried brewers' yeast and wheat germ, a number of brands of which have been accepted by the Council on Foods (THE JOURNAL, Sept. 12, 1931, p. 780; Aug. 1, 1931, p. 321; Jan. 2, 1937, p. 47; June 30, 1934, p. 2187; Oct. 2, 1937, p. 1127). Quantitative data regarding the vitamin content of a large number of common foods may be found in the recently published U. S. Department of Agriculture Miscellaneous Publication 275, entitled "The Vitamin Content of Foods," by Ester Peterson Daniel and Hazel P. Munsell. A second printing of this pamphlet has been made and is now available for distribution. Another source of quantitative data concerning the mineral and vitamin content of foods is "The Laboratory Handbook for Dietetics," by Mary S. Rose, fourth edition, New York, Macmillan Company.

SALIVARY AND SERUMAL CALCULI

To the Editor:—What is the cause for a secretion of salivary and serumal calculi on the lingual surfaces of the lower anterior teeth? Constant scaling removes the deposits for a short time, thus requiring almost weekly visits to the dentist. The calcium and phosphorus content of the blood is normal. There is no evidence of endocrine disturbance. There is prognathism of the lower jaw.

M.D., New York.

ANSWER.—Salivary and serumal calculi are composed principally of a calcoglobulin which is deposited on the surfaces of the teeth. With the disintegration of protein a hard residue of mineral is left. Salivary calculus occurs on the surfaces of the teeth above the gum line. It is most frequently found in proximity to the orifices of the salivary glands, namely, the lingual surfaces of the lower incisor teeth and the buccal surfaces of the upper molar teeth.

Dr. G. V. Black, following experiments in his own and the mouths of others, was able to produce deposits of salivary calculus apparently related directly to the diet.

In well nourished persons an excessive amount of protein and mineral frequently leaves deposits of this sort. Large quantities of milk and rich foods seem to predispose to the condition. Dr. Black was able to produce a deposit by the drinking of one glass of milk over and above a daily dietary intake that was not productive of calculus formation. If the diet is well balanced, merely a reduction in total quantity is often sufficient to reduce the deposits.

Serumal calculus forms beneath the gingival margin. It is often associated with pockets that form with peridental disease. There is still considerable controversy concerning whether this deposit is the cause of the condition or merely coexistent with it. The chemical composition is similar to that of salivary calculus if not identical with it, its dark color being due to inclusion of blood pigment. It is probable that serumal calculus occurs because of the opportunity offered by the pyorrhea pocket and in turn contributes through irritation to the progress of this condition.

In most instances the quantity of deposits of both types of calculus can be controlled by careful regulation of the diet. The teeth should be kept scaled and as free from irritation of the soft tissue as possible in the meantime.

HYPERTENSION IN YOUNG FEMALE

To the Editor:—Please discuss treatment of hypertension in a young female without any demonstrable abnormalities other than a mild secondary anemia.

M.D., Iowa.

ANSWER.—The treatment of hypertensive arterial disease is highly individualized. As adequate therapy must be based on knowledge of the causation, and as the provoking cause in hypertensive disease varies with each patient, the individual character of proper treatment becomes apparent. Accurate diagnosis must be the prelude to successful therapy; this implies not only the discovery of hypertension but also consideration of the etiology (the importance of constitutional or familial—predisposing—factors in relation to precipitating or provoking factors such as possible plumbism, occult nephritis or endocrine disorders) and a quantitative evaluation of the extent of arteriolar damage.

Assuming that the statement that there are no "demonstrable abnormalities other than a mild secondary anemia" is literally correct and not the result of failure to search for disturbances, there are two significant possibilities. The severity and progressiveness of hypertensive arterial disease is usually in inverse ratio to the age of onset. In young persons hypertension is usually associated with severe renal injury; if this patient is quite well otherwise, one must consider congenital coarctation of the aorta as a possible reason for the hypertension in the arms. This may be readily proved or disproved; such stenosis of the aorta is the only condition in which the arterial tension in the legs (measured at the popliteal space) is lower than in the arms. Although coarctation is rare, it must always be ruled out, especially in young patients who appear surprisingly well despite their hypertension. The second, and more probable, reason for the hypertension is its possible association with the anemia. The query does not state the reason for this anemia and thus it must be assumed that the reason was undiscovered. It is quite probable that the patient has a chronic nephritis with little or no proteinuria but functional impairment. This can and should be determined by renal function tests. Such renal function studies are indicated in every instance of arterial hypertension. The association of hypertension with anemia not necessarily of renal origin is not uncommon. It has been frequently observed that as the hemoglobin content of the blood is increased by appropriate therapy

(liver, iron) the arterial tension comes down to normal or nearly normal levels. This association occurs so often that it is probably not coincidental.

Thus, correction of anemia is of great importance in treating hypertensive arterial disease. Ample rest, the appropriate use of sedatives to insure relaxation, liberal fluid intake (from 2.5 to 3 liters in twenty-four hours), a balanced dietary with avoidance of condiments, spices, and more than the normal amount of salt, study of the personality problems and calm reassurance are significant adjuncts to therapy. If the etiology remains wholly obscure, the only direct therapy possible is through the use of mild long continued arterial sedatives. This is often of the greatest value, when no active etiologic irritants are operative. Arteriolar sedation sometimes can be obtained with small doses (0.0015 Gm. or one-fourth grain) of erythrol tetranitrate three times a day or with 0.6 Gm. (10 grains) of bismuth subnitrate thrice daily. Sodium or potassium thiocyanate is not safely used unless the patient is carefully observed, with frequent determinations of the thiocyanate concentration in the blood.

POSSIBLE ALBUMINURIA FROM MASCARA

To the Editor:—A woman, aged 21, single, presents myriads of symmetrical punctate hemorrhages in the skin about the eyes. The eyes themselves are normal; although prior to the appearance of the eruption there was a sensation of heat and prickling in this region. She uses rouge and, in addition, "Mascara" to her eyelids weekly. I first examined her in September 1935. At that time she complained of severe abdominal pain without any definite localization and with normal pulse and temperature. Urinalysis was negative except for a specific gravity of 1.027 and a considerable amount of albumin; there were no casts. The blood pressure was then and is now about 120 systolic, 70 diastolic. There have been no further intra-abdominal manifestations since September 1935. The patient's younger sister also has practically the same condition; namely, an albuminuria without casts or hypertension. Have you received reports of similar conditions following the use of Mascara about the eyelids?

RICHARD B. OLESON, M.D., Lombard, Ill.

ANSWER.—Mascara is a Spanish word meaning masquerader and is applied to many preparations for the eyebrows and eyelashes to darken them. Their composition varies from combinations in which lampblack is the pigment to those containing dangerous dyes. A number of reports have appeared in the last few years of severe reactions to dyes used on the eyebrows and lashes. (Greenbaum, S. S.: Dermatoconjunctivitis Due to Lash-Lure, an Eyelash and Eyebrow Dye, THE JOURNAL, July 29, 1933, p. 363.)

That even lampblack may cause trouble is evidenced by the query (THE JOURNAL, March 10, 1917, p. 799) asking about the cause of a dermatitis on the arms of men who shoveled lampblack made from California fuel oil. The eruption appeared only when the men perspired. It was ascribed to the fumes of higher hydrocarbons, as benzene and naphthalene given off by lampblack when heated.

Petechial eruptions are often due to absorbed drugs, rarely to local applications. If the eruption described in the query was due to the Mascara it may have been a result of absorption. The dyes used in the more complicated forms of Mascara are aniline dyes and both they and the higher hydrocarbons in lampblack might cause a petechial eruption. To prove this relation, further experiments would be needed; but their advisability for the patient is doubtful. Other possible sources of a purpuric eruption should be sought, the spleen and liver examined, a complete blood count with platelet count made, and the coagulation time and bleeding time tested.

Albumin in the urine without casts can occur in (1) orthostatic albuminuria, in which the amount is small in the morning and increases as the day lengthens; (2) alimentary albuminuria, increased by ingestion of albuminous foods; (3) albuminuria due to chronic infection, chiefly staphylococcus or syphilis; (4) acute syphilitic nephritis, and (5) nephrosis.

Burden (Persistent Functional Albuminuria, *Am. J. M. Sc.* **188**:242 [Aug.] 1934) examined 3,642 male students at the University of Pennsylvania and found that 6.4 per cent had persistent albuminuria. That this could not correctly be called functional was shown by the occasional occurrence of hyaline and granular casts in 20.3 per cent. A careful survey of this group showed little departure from the normal except that in 12 per cent there was a history of cardiorenal disease in one parent. Results for calcium in Burden's group were normal or on the high side of normal. It was reasoned that that does not preclude a low diffusible calcium fraction, favoring increased permeability of the glomerular membranes. Calcium gluconate was given by mouth, 4 Gm. four times a day for two weeks, to sixteen patients. In five there was no change. Six showed a definite decrease in the amount of albuminuria and five recovered entirely. Four of the latter were still albumin free a year later.

ACUTE INTESTINAL OBSTRUCTION?

To the Editor:—A man, aged 56, became exhausted after a busy and sleepless week preparing for a trip. The morning he was to depart he drank some brandy (as he has done all of the past twenty years), followed by some coffee. Almost at once he became nauseated and vomited. He then had some abdominal cramps. He had had no previous abdominal complaints. Following vomiting he felt somewhat better and decided to go on the trip anyway. Throughout the day the abdominal cramps gradually increased in severity and frequency. He was required to stop the automobile several times so that he could vomit. I first saw him at 7 p. m. At that time he was writhing with pain. The abdomen was distended with gas and was tympanitic. It was tender throughout without guarding, with the most marked tenderness to the left and below the umbilicus, with dulness in this area. No fluid was present. He was belching foul gas and at frequent intervals vomited or attempted to do so. The temperature was 97 F., the pulse 110. He had passed no gas or fecal material by rectum during the past twenty-four hours. He was encouraged to defecate and passed a hard dry stool, but no gas. He was given an enema, with return of practically clear fluid but no gas. He was given a hypodermic of morphine in order that he might be moved by ambulance 20 miles to the hospital for observation. He had almost no pain during the night. The following day, at 1 p. m., cramps and nausea began again. These became severe at once, and visible peristalsis was present. He still had passed no gas by rectum. His temperature at that time was 99.8 and pulse 110. Exploration was decided on and done under ether. A midline suprapubic incision was made and a much dilated, red, irritated bowel extruded from the wound. Clear fluid, 500 cc., was also present. Several small flakes of material much as seen in perforated ulcer were present. The entire colon was normal. The small intestine was inspected throughout its entire length. The bowel was distended to within three feet of the ileocecal valve. From this point on it was collapsed and not irritated. Gas could be made to pass easily from the distended to the collapsed bowel. It appeared as though there had been an obstruction at this point but that it had been relieved. No diverticula were found. The stomach and duodenum were explored; no perforations were found. The kidneys, gallbladder, liver and spleen were normal. The abdomen was closed with drainage. Twelve hours after operation he began to pass gas by rectum. He had a febrile reaction to 101 F. on the second day following intravenous dextrose, but since that time his temperature has been normal. Enemas have brought large quantities of gas and fecal material. He has taken liquids and some solids without nausea or vomiting. Distention has disappeared. My impression is that he had a volvulus of the small intestine which relieved itself spontaneously under the ether. I would appreciate your opinion.

M.D., Arizona.

ANSWER.—This case is unusual in that it does not definitely fit into any typical clinical picture. It would seem that the patient was suffering from an acute obstructive process and it is difficult to understand why such a process of more than twenty-four hours' duration would not leave more definite evidence. It is unusual to have volvulus of the small intestine without some previous operation or some acute inflammatory process which had produced anchoring adhesions. Intra-abdominal hernias, such as can occur in the intra-sigmoidal, paracecal and paraduodenal fossae, might explain the condition, or perhaps a hernia through some other exaggerated mesenteric fold or through a congenital defect, such as has been described by Treves. Prutz collected thirty-six instances of this type.

Another possibility, which would seem rather remote, is that of dynamic ileus, such as formerly was seen not uncommonly in acute lead poisoning or in certain food poisonings. In this condition a small section of the small intestine becomes spastically obstructed, producing the picture of intestinal obstruction even to the development of some fluid within the abdominal cavity, but without infection.

PERSISTENT SHREDS IN URINE AFTER PROSTATIC RESECTION

To the Editor:—I have an infection of the urinary tract following a transurethral resection. It is characterized by shreds, alkaline urine and phosphaturia, and relief is obtained only in a combination of an acid ash diet, excessive water drinking and acidification with ammonium chloride. What is the cause of the shreds and how is one to get rid of them? Are they the cause of the urine becoming alkaline? Why does the urine become alkaline, phosphatic and cloudy if not voided frequently? Why, on an acid ash diet, forced fluids but without acidification, is the urine still either neutral or alkaline? Granted that the only way to keep the urine clear and normal in reaction is to keep indefinitely on an acid ash diet, copious drinking and acidification, is it compatible with life and health? Is a neutral reaction normal? Would you indicate the sources where I could look up this subject?

ROBERT FISHER, M.D., Bronx, New York.

ANSWER.—The persistence of infection with alkaline urine and shreds following transurethral resection is often caused by residual prostatic tissue. It is not stated what bacteria have been found in the urine on culture. In some cases infection of this kind is the result of Proteus or Salmonella; sometimes these bacteria cause the urine to become so alkaline that it is impossible to acidify it by ordinary methods. Recent experience has shown that sulfanilamide will eliminate both Proteus and Salmonella in the majority of cases. If it does not, another cystoscopic examination should be made by some experienced

urologist and if residual prostatic tissue remains it should be removed. This can usually be done by a competent transurethral resection.

If areas of incrustation are found in the base of the bladder, these can be treated either by curettage and applications of 20 per cent silver nitrate or by continuous irrigation with acetic acid over a period of from twenty-four to forty-eight hours.

LIQUID DIET FOR TUBE FEEDING

To the Editor:—My wife, owing to a paralysis of the muscles of deglutition, is being fed through a Levine tube, sizes 14 and 16. Knowing that her time is limited and wishing to make her as comfortable as possible, I should like to maintain her nutrition in the best possible way. Could you outline as specifically as possible a well balanced liquid diet that would have an adequate caloric and vitamin content?

M.D., Oklahoma.

ANSWER.—The cardinal principle of tube feeding is to give the body sufficient calories and at the same time attempt to maintain a balance. The following is a list of foods from which a menu can be planned:

Acid milks
Albumin fruit juices
Albumin water (1 or 2 whites of eggs to a glass of water)
Almond milk
Applesauce
Apricots
Barley water
Beans, lima
Beef juice
Beets
Bemax
Black coffee
Bouillon
Butter
Buttermilk
Carrots
Cereal waters
Chicken broth
Chocolate
Clear and cream soups
Cocoa
Cod liver oil
Cornmeal
Cream
Cream of wheat
Dextri-Maltose
Dryco
Eggs (raw)
Farina
Fruit juices
Glucose (10 per cent solution)
Honey
Karo
Klim
Lactose (10 to 20 per cent solution)
Maple syrup
Malted milk
Milk, cow's or goat's
Oatmeal gruel
Olive oil
Orange albumin (1 or 2 whites of eggs with juice of an orange in equal parts of water)
Parsnips
Peas
Peptone solution (20 to 40 per cent)
Peptonized milk
Plain milk
Potato, boiled, sweet or white
Prunes
Pumpkin
Ralston
Rice
Salt
Spinach
Strained cereals
Strained fruits
Strained vegetables
Sugar
Tea, clear
Tomato juice
Turnip
Vegetable soup
Wheatena
Whites of eggs

All food in solid form must be puréed and strained and milk or other diluent added to make proper consistency for passage through the tube. Many commercial firms offer excellent canned puréed or strained cereals, vegetables and fruits, which will obviate much household labor.

It is customary to make combinations of these foods, depending on volumetric and caloric necessities. Alcohol and caffeine (in the form of coffee) are at times indicated. The caloric yield per diem can readily be calculated, and the volumetric intake can be restricted or amplified as desired.

The introduction of a diet too high in carbohydrates is not indicated, as the customary oral digestion is absent; hence the addition of too much carbohydrate may produce untoward intestinal symptoms.

PENTACHLORPHENOL

To the Editor:—Are you able to give me any information concerning the water soluble sodium salt of pentachlorphenol, an agent which was used as a fungicide in the preparation of lumber and other forest products? I am especially interested in knowing the effects of this agent on the skin, and suitable means of prevention of skin irritations.

ALLEN D. LAZENBY, M.D., Baltimore.

ANSWER.—Published material on the toxicity of the sodium salts of pentachlorphenol (C_6Cl_5ONa) is most meager. Only on the basis of similarity to other chlorinated coal tar derivatives is it possible to take any stand as to the toxic properties of this chemical. Iwanowski and Turske (*Chemical Markets* **32**:327, 1933) have described the chemical preparation of certain sodium salts of chlorphenol. From such chemical description, it is reasonable to believe that this fungicide in aqueous solution is so stable that it is unlikely that decomposition will take place, even when the solutions are heated. On this account, whatever ill effects may be produced in the procedure of wood treatment are to be attributed to the chemical itself. In view of the highly toxic properties of chlorinated naphthalenes, it is desirable to regard all chlorinated phenols with apprehension until greater experience may make this concern unnecessary. It is predictable that two types of dermatitis may be produced by chlorinated phenols, one the usual diffuse chemical rash and second "chlor-acne." Possibly more information may be obtained from the Forest Product Laboratories of the United States Department of Agriculture.

HYPERTENSION

To the Editor:—A white man, aged 78, came to me two months ago complaining of pain in the right shoulder radiating down the right arm, sharp, shooting pains in the back (lumbar region) and vertigo. Physical examination at this time was negative except for a blood pressure of 210 systolic, 100 diastolic. I prescribed elixir of potassium thiocyanate 1 drachm (4 cc.) three times a day and elixir of five bromides every four hours. On this treatment his pains vanished and his blood pressure dropped gradually to 145/90. I gradually cut the dosage on the cyanates as the pressure fell so that it was omitted entirely two weeks later when the blood pressure was 150/85. At this time the heart action was not so good, as evidenced by distant heart sounds. I proceeded to digitalize the patient. Immediately his blood pressure went from 165/95 to 195/105 and the patient felt better than he had at all. Since that time his blood pressure has been variable, ranging from 145/90 to 215/110. Last week an electrocardiogram was made, and this was the report: The first lead was practically normal with the exception of a slurring QRS complex upright of normal amplitude; the second lead contained considerable slurring, more than the first, with a widening of the QRS complex with a deflection of the QRS complex; the T wave was normal. In the third lead there was still more slurring than in the previous two leads, with marked widening and complete deflection of the QRS complex. There is also a deflection of the T wave in the third lead. Urine examinations until three weeks ago were negative but since that time have been showing a strong trace of albumin. I have been advised to discontinue the digitalis on this patient because it is "like whipping a tired horse." What would you advise about this and further treatment?

M.D., Georgia.

ANSWER.—The experience with this patient is a common one. Many patients suffering from long continued hypertension are distressed when any therapeutic measure successfully lowers the pressure. The electrocardiogram is consistent with the change seen in hearts following hypertension. Digitalis is indicated in these patients when there is evidence of a cardiac failure. It should be used to the point at which desired results are obtained. To this treatment might be added theobromine with sodium salicylate or one of the related compounds. The activity of the patient should be restricted to a point below that which produces dyspnea.

CONGENITAL SYPHILIS WITH NEGATIVE SEROLOGIC REACTION OF MOTHER

To the Editor:—A breast-fed infant, 3 months old, shows the typical signs of florid congenital syphilis, with the history that symptoms first became evident at 1 month of age. Wassermann reaction is reported four plus on the baby, but both the Wassermann and the Kahn reaction of the mother are negative. In addition the mother shows no signs of the disease but reports a rash of a suspicious nature that appeared all over her body during the last month of pregnancy. This is her first marriage and first pregnancy. What should be done for the mother in the way of care and treatment? Could this be a spontaneous cure brought about by pregnancy? How can this be proved? I have allowed the baby to continue at the breast. Is this proper judgment? The father is not available for examination. Colles's law has been so variously interpreted that I am somewhat confused concerning the status of a case like this.

M.D., California.

ANSWER.—In this country, physicians still hold to the concept of the maternal transmission of syphilis, believing that paternal transmission, that is, from the father directly to the offspring, is impossible. If the diagnosis of congenital syphilis in the baby is accepted as accurate, the following explanations of the situation are worthy of consideration: 1. The child may have acquired syphilis at the time of birth or shortly thereafter from some source other than the mother. 2. The mother may have a latent syphilis with a negative serologic reaction (17 per cent of these women have syphilitic children). 3. There may be a possible technical error in the test of the mother, which would warrant repetition of the blood tests from month to month. 4. The possibility of spontaneous cure by pregnancy is remote and cannot be proved, and it can be presumed to have taken place only after an observation period of five years has elapsed. With regard to treatment of the mother, two courses are open: to continue with observation, making an effort to establish the diagnosis of syphilis by serologic tests or otherwise, or to consider her as having latent syphilis and carry out treatment accordingly. If the latter plan is undertaken, as it probably should be, as she is apparently a young woman the treatment must be intensive in order to prevent a subsequent pregnancy terminating in another syphilitic child. There is no objection to permitting the child to remain at the breast if it is her child.

The evidence favors a diagnosis of latency in the mother rather than spontaneous cure as a result of the pregnancy. Further clinical and serologic search is necessary to establish the exact status of the mother.

TRANSMISSION OF TUBERCULOSIS

To the Editor:—A woman, aged 30, was diagnosed as having tuberculosis fifteen years ago and advised to take sanatorium treatment. This she did not do. She has been married and divorced and has worked all the time since the age of 17 or 18, although her general health has not been good. She is thinking of marrying again and wants to make sure that she is free from the disease and incapable of transmitting tuberculosis to any one by kissing or in any way. She had an appendectomy about five years ago and the diagnosis was made at that time of intestinal tuberculosis. About two years ago she was passing blood from the urethra at the end of urination and still does so at intervals. She had no other genito-urinary symptoms, although two years ago she had pain, aggravated by pressure over the right kidney and ureter. About ten days ago she had a Mantoux test with 0.5 mg. of old tuberculin, which was negative, followed by another Mantoux test with 1 mg. of old tuberculin, which also was negative. The x-ray examination showed that both diaphragms were smooth. The gastrophrenic angles were clear. The heart and aorta were of normal size and position There were multiple calcified Ghon foci in the hilar zone of the right upper lobe; the left hilus was within normal limits. There was no infiltration noted in either lung field. The diagnosis was absence of active pulmonary tuberculosis. Would you consider the patient free from active tuberculosis in all parts of her body? Would you consider it possible for her to transmit tuberculosis to any one by any method? Please explain Ghon foci.

M.D., Illinois.

ANSWER.—The recent Mantoux tests with negative results should be repeated with larger doses of tuberculin—from 1 to 3 mg. of old tuberculin or 0.005 mg. of the purified protein derivative of tuberculin. If the tests continue to be negative, she may be considered to be free from active tuberculosis and incapable of transmitting tuberculosis to any one.

However, the diagnosis of intestinal tuberculosis five years ago and the hematuria, which may be due to renal tuberculosis, are not in accord with negative tuberculin reactions, although, in rare instances, this might occur.

The Ghon foci on the x-ray film are calcified tuberculous tracheobronchial lymph nodes associated with the primary tubercle in the lung.

RECOVERY FROM PULMONARY TUBERCULOSIS

To the Editor:—A white woman, aged 35, has bilateral pulmonary tuberculosis. X-ray examination of the right side shows no activity. On the left side, three cavities were present in December 1936. Pneumothorax has been instituted and the cavities are completely collapsed. The weight has increased from 88 to 115 pounds (from 40 to 52 Kg.); there is no sputum; the temperature is normal; the pulse rate is 76 or less. Clinically there is much improvement. Is there any reason why she should not be made partially ambulatory?

M.D., Indiana.

ANSWER.—There is no hard and fast rule when the patient shall be allowed to get out of bed for any length of time. If the temperature has been persistently normal for some time, the patient may be allowed to sit in a chair for half an hour a day, the period of time of sitting up being gradually extended. Then limited walking exercises may be attempted. At first only five or ten minutes a day should be taken, and if there are no ill effects the walking exercises may be increased gradually over several weeks until the patient is taking two or three hours of exercise daily.

The pneumothorax treatment begun in December 1936 should be continued and maintained for at least two years if possible, so that the cavities in the left lung may remain permanently collapsed.

BLISTER TREATMENT OF NARCOTIC ADDICTION

To the Editor:—A physician (an addict), just before his death, gave to a friend a treatment which he claimed would cure any dope addict of the habit with one application of the treatment. The physician claimed that he cured himself twice but that he began using the narcotics again because he had a cancer of the jaw. I have discouraged this friend concerning the treatment, as I could not see logic in such a procedure. The treatment is as follows: Place a plaster of Spanish fly on the anterior abdominal wall. When a blister has formed, remove the plaster so as not to break the blister. With a hypodermic syringe draw the fluid from the blister and inject it into the buttock. One treatment is supposed to cure the worst addict. Is there any rationale for such treatment? What are the dangers accompanying such a procedure, and what is your opinion as to the efficacy?

M.D., Florida.

ANSWER.—The treatment is based on the theory that there is an antidotal toxic substance in the serum of addicts. It was originated by Dr. Modinos of Java. It has been extensively used throughout the Orient during the past few years to help reduce the acute withdrawal symptoms, principally in the treatment of opium smokers. In addition to the serum injection therapy the patient is given, by mouth, tincture of opium with tincture of belladonna and nux vomica. The day after each injection of the serum a new blister is raised. This is repeated until three or four injections have been given. In the meantime the tincture of opium is continued in rapidly diminishing doses. Also phenobarbital and pentobarbital sodium are given to obtain sleep. The bowels are kept open with compound cathartic pills. It is reported that this allows a much more rapid and less painful withdrawal of the opiate. There is no convincing evidence of an antidotal toxin being present in the serum of narcotic addicts—it is pure assumption. There would be no danger from the treatment if strict asepsis should be maintained. Its efficacy would be in direct proportion to the patient's faith in its efficacy.

BITTERS AND ANGOSTURA BITTERS

To the Editor:—Is there any justification for such concoctions as bitters? What in them is of especial value to any particular constitution, whether in the tropics or elsewhere, that would be a recommendation for their use internally? In the case of a prominent product, Angostura Bitters, there is a high alcoholic content; the label says 45 per cent. Perhaps the chemical laboratories already know the component parts comprising this mixture and will disclose the composition. I should like very much to know what the product is.

MORTIMER A. LASKY, M.D., Brooklyn.

ANSWER.—Bitters are largely a "matter of taste"; i. e., they are likely to stimulate appetite and digestion for those who relish this taste. When appetite and digestion are languid, especially in hot weather, a dose of bitters taken before a meal may rouse the stomach to more satisfactory work. Angostura bitters may owe its value in addition to the presence of cinchona bark; and it may be this which caused the explorer von Humboldt to have been so much benefited that he brought it to Europe in 1839. This liqueur was first devised in 1832 by Surg. Gen. J. H. B. Siegart of Venezuela, and it is still made according to the original formula by his descendants at Trinidad. A similar article may be obtained according to the Chemist's Recipe Book (published by the *Chemist and Druggist*, 28 Essex Street, Strand, London, W. C.) from the following formula:

Angostura bark	4 ounces
Cinchona bark	2 ounces
Bitter orange peel	2 ounces
Galangal root	10 drachms
Cinnamon	10 drachms
Cassia buds	10 drachms
Red sandalwood	10 drachms
Cardamom seeds	½ ounce
Gentian root	3 drachms
Alcohol (50 per cent)	1 gallon
Rum	1 gallon
Macerate for a week and in the filtrate dissolve	
Sugar	2 pounds
Oil of cognac	20 minims

HYPERPYREXIA FROM CARBON MONOXIDE OR INFECTION

To the Editor:—March 1 a Negro, aged 31, was overcome by carbon monoxide gas from a gasoline engine. He was unconscious for a considerable time and it appeared that he would not recover. Since then he has had frequent chills and high fever, which last for two or three days with periods of remission. This has happened eight or ten times since the accident. He complains of gastric disturbances with tightening in his chest and abdomen. Exercise and the hot sun seem to precipitate an attack of chills and fever. Laboratory work including blood counts, examination for malaria, the Wassermann test and a smear for white and red blood cells have all given normal results. Physical examination gives normal results. If you have a suggestion to offer in this case I could appreciate it.

M.D., Georgia.

ANSWER.—The sequelae of severe carbon monoxide poisoning in which the patient has been unconscious may be represented by highly different bizarre manifestations. One patient may present an extensive gangrene, another total blindness, a third pulmonary hemorrhage, a fourth nephritis. Therefore it would not be remarkable if a patient had hyperpyrexia. In many instances the temperature is low, but high temperatures, lasting from a day to two or three weeks, are well known. The cause of the temperature increase may be found in postasphyxiation infection, such as pneumonia, but when the temperature rise is sudden and high, this occurrence is usually related to hemorrhagic insult in the brain. The occurrence in the present instance of intermittent high temperature and chills is less characteristic, particularly when these recurrences have persisted over a period of months. If the temperature rises were substantially continuous, it would be within reason to suspect direct hemorrhagic changes in the portion of the brain connected with temperature control. Contrariwise, it is believed that explanation is to be found in some other portion of the body. Intermittent chills, with elevated temperature in a Georgian, first suggests malaria, although this apparently has been ruled out. Pyelitis is a possibility, as is also low grade infection of the respiratory tract. It is suggested that additional effort be made to associate the occurrence described with an infectious process. If these possibilities are exhausted, it becomes reasonable to accept this condition as an unusual sequel of severe acute carbon monoxide poisoning, traceable to vascular changes within the brain or its covering.

THERAPY IN PULMONARY MONILIASIS

To the Editor:—Please inform me as to the amount, the frequency of administration, and the length of time the medication can be continued when treating a case of pulmonary moniliasis with (*a*) thymol, (*b*) gentian violet and (*c*) methylene blue.

PAUL K. JENKINS, M.D., Miami Beach, Fla.

ANSWER.—Such information of the details of the substances in pulmonary moniliasis does not seem to be readily available. Indeed, iodide seems to be the remedy of choice; it is admitted that it fails in some cases. The following dosages of these various agents have been employed chiefly for other purposes:

(*a*) A total dose of 2 Gm. of thymol is considered safe for adults, best given divided into three portions, taken an hour apart and administered in the form of fine powder in 0.30 Gm. capsules. Fats, oils and alcohol must be avoided during treatment. The treatment may be repeated at weekly intervals. Intramuscular injection of from 2 to 3 cc. of a 6 per cent oily solution has been administered daily for seven days.

(*b*) Gentian violet has been given by mouth in doses of 0.065 Gm. administered in capsules three times daily. Intravenous injection of 5 mg. per kilogram of body weight in 0.5 per cent solution has been given, repeated in five hours if necessary.

(*c*) Methylene blue may be given in doses of from 0.4 to 0.6 Gm. four times daily for many days. It may be injected intravenously in quantities of 50 cc. of 1 per cent solution, repeated at intervals up to a total of 200 cc. Cyanosis may occur as the result of the formation of methemoglobin, which may require blood transfusion.

IMPERFORATE ANUS

To the Editor:—A baby girl 4 months old has a cloaca. The birth weight was 6 pounds (2.7 Kg.); the present weight is 12 pounds 8 ounces (5.6 Kg.). What is the general opinion as to the time of operability or perforating the anus?

M.D., Wyoming.

ANSWER.—If the baby girl has an opening of the terminal bowel into the vagina and the bowel contents are discharging freely, it is better to wait until the child has reached the age of 6 to 8 years before the bowel is returned to its normal site. If, however, the opening into the vagina is so small that partial obstruction results, either the opening should be enlarged where it is by dilation or by a minor plastic procedure, when the opening of the bowel is in the vagina at the posterior fourchette. Occasionally as the child develops the rectum and vagina will grow apart. While this is not a common occurrence it nevertheless justifies waiting for a few years before any major attempt is carried out to replace the anus to its normal site.

MICROCOCCUS CATARRHALIS IN URINARY INFECTIONS

To the Editor:—Do you know any drug effective against Micrococcus catarrhalis in the male genito-urinary tract?

J. R. TUCKER, M.D., Williamsburg, Va.

ANSWER.—Micrococcus catarrhalis is rare as a cause of genito-urinary infections. It is impossible to diagnose the condition by Gram's stain, as the organism resembles any degenerating or otherwise poorly staining staphylococcus. Growth on ordinary culture mediums is poor. Methods devised to grow cultures of the gonococcus will give cultures of Micrococcus catarrhalis. The colonies will be three or four times as large as the gonococcus and show an intense oxydase reaction.

Since sulfanilamide may have a beneficial effect on other members of the Neisseria group (THE JOURNAL, May 29, 1937, p. 1855 and April 24, p. 1407) it may be tried for this organism. There is as yet no standard dosage, but apparently the best results have been obtained by using rather large doses. Reactions are common and may be dangerous. Close supervision by the physician is necessary. A description of sulfanilamide appears in THE JOURNAL, November 30, page 1454.

Neoarsphenamine 0.3 Gm. intravenously is also of value. Two or three doses at weekly intervals should be used.

TULCA LENSES

In THE JOURNAL, Oct. 23, 1937, page 1384, appeared a query and answer on the subject of Tulca Unbreakable Lenses. In the answer it was stated that, when dropped into boiling water, Tulca lenses became immediately distorted. Information has since been supplied that a lens has been suspended in boiling water for ten seconds and when withdrawn was tested on a Zeiss refractionometer and the strength of the lens was found to be identical with its original correction. In connection with the statement that the lenses catch fire rapidly and burn with the same flame as celluloid, it has been found that celluloid ignited in one-fourth second and burned with the characteristic celluloid flame whereas Tulca lens material ignited in four and one-fourth seconds and burned with a small flame, showing the characteristic yellow of carbon with a distinct hydrogen cone.—THE EDITOR.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, January 8, page 150.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Examinations will be held in all centers where there is a Class A medical school and five or more candidates who wish to write the examination, Feb. 14-16, May 9-11 (limited to a few centers), June 20-22, and Sept. 12-14. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written examination for Group B applicants* will be held in various cities throughout the country April 16. *Applications due Feb. 15. Oral examinations for Group A and B applicants* will be held at San Francisco June 13-14. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: Examinations will be held in various centers of the United States and Canada, Feb. 14. Chairman, Dr. Walter L. Bierring, 406 Sixth Ave., Suite 1210, Des Moines, Iowa.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written examinations and review of case histories for Group B candidates* will be held in various cities of the United States and Canada, Feb. 5. *General oral, clinical and pathological examinations for all candidates (Groups A and B)* will be conducted in San Francisco, June 13-14. *Application for admission to Group A examinations must be on file before April 1.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: San Francisco, June 13; Washington, D. C., Oct. 8; Oklahoma City, Nov. 15. *All applications should be filed immediately and case reports, in duplicate, must be filed not later than sixty days before the date of examination.* Sec., Dr. John Green, 3720 Washington Blvd., St. Louis, Mo.

AMERICAN BOARD OF OTOLARYNGOLOGY: San Francisco, June 10-11. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF RADIOLOGY: San Francisco, June 10-12. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Maine November Examination

Dr. Adam P. Leighton, secretary, Maine Board of Registration of Medicine, reports the written examination held at Portland, Nov. 9-10, 1937. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Eighteen candidates were examined, 17 of whom passed and one failed. Four physicians were licensed by reciprocity and one physician was licensed by endorsement after an oral examination. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Boston University School of Medicine		(1934)	83, (1936) 82, 85
Harvard University Medical School		(1928)	78
Tufts College Medical School		(1914)	78, (1928) 79, (1936) 86, 86, (1937) 80, 81
Columbia University College of Physicians and Surgeons		(1934)	85
New York Medical College and Flower Hospital		(1936)	83
University of Pennsylvania School of Medicine		(1937)	79
McGill University Faculty of Medicine		(1909) 76, (1932)	81
University of Montreal Faculty of Medicine		(1937)	76
Pennsylvania Medical School, Shanghai, China		(1931)	75.5

School	FAILED	Year Grad.	Per Cent
National University of Athens School of Medicine		(1935)*	60

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Michigan Medical School		(1924)	California
Eclectic Medical Institute, Ohio		(1905)	Ohio
Temple University School of Medicine		(1936)	Penna.
University of Vermont College of Medicine		(1936)	Vermont

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1931)	N. B. M. Ex.

* Verification of graduation in process.

Ohio Reciprocity and Endorsement Report

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports 24 physicians licensed by reciprocity and 5 physicians licensed by endorsement on Oct. 5, 1937. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1935)	Colorado
George Washington University School of Medicine		(1916)	Dist. Colum.
Georgetown University School of Medicine		(1898)	Dist. Colum.
Loyola University School of Medicine		(1933)	Michigan
University of Illinois College of Medicine		(1936)	Michigan
State University of Iowa College of Medicine		(1936)	Iowa
University of Kansas School of Medicine		(1935, 2)	Kansas
University of Louisville School of Medicine		(1935)	California, Kentucky
Tulane University of Louisiana Medical Department		(1911)	Louisiana

Harvard University Medical School	(1933)	Maryland
University of Michigan Medical School	(1930)	Michigan
St. Louis University School of Medicine	(1934), (1936, 3)	Missouri
New York Homeopathic Medical College and Flower Hospital	(1925), (1935)	New York
University of Pittsburgh School of Medicine	(1916), (1934)	Penna.
Meharry Medical College	(1936)	Tennessee
University of Tennessee College of Medicine	(1931)	Tennessee
Medical College of Virginia	(1932)	W. Virginia

LICENSED BY ENDORSEMENT

School	Year Grad.	Endorsement of
Georgetown University School of Medicine	(1936)	N. B. M. Ex.
Harvard University Medical School	(1929), (1931)	N. B. M. Ex.
Cornell University Medical College	(1933)	N. B. M. Ex.
Woman's Medical College of Pennsylvania	(1934)	N. B. M. Ex.

Book Notices

Recent Advances in Industrial Hygiene and Medicine. By T. M. Ling, M.A., B.M., M.R.C.P., Senior Medical Officer, Bristol Police. Foreword by J. A. Nixon, C.M.G., M.D., F.R.C.P., Member of the Industrial Health Research Board, Medical Research Council. Cloth. Price, $3.50. Pp. 212, with 29 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1937.

Industrial hygiene has in recent years come to assume an important place both in medicine and in industry. It will in future form an integral part in the medical curriculum. In this book Dr. Ling has brought together the modern advances which have been made in industrial hygiene. The recognition, prevention and cure of the occupational diseases known, say, thirty years ago and taught to the medical students of that generation form a very small part of industrial medicine of the present day. The occupational selection of employees is a problem of prime importance both to employers and to workers. Dr. Ling discusses psychic and physical aptitudes for employment in all their bearings, with wide knowledge of the progress that has been made and with considerable caution. Industrial sickness is examined from the point of view not only of engagement in dangerous trades but of industry in general. The effect of hours of work, rest pauses, refreshment intervals and wage levels on the incidence of sickness and absence are thoughtfully considered, as well as such factors as ventilation, humidity, air conditioning and lighting. The incidence of accidents, their treatment and rehabilitation after injury are fully dealt with and the valuable lessons to be learned from Bohler's clinic in Vienna are justly insisted on. Industrial fatigue, the neuroses and the well known occupational diseases all come under review. As a compendium of all the latest work, Dr. Ling's book will recommend itself to all medical practitioners, and especially to industrial physicians and medical referees under the workmen's compensation act—to employers of labor, to welfare workers, to lawyers engaged in compensation cases and to judges sitting as arbitrators in such cases.

Nouvelle pratique dermatologique. Publiée par MM. Darier, Sabouraud, Gougerot, Milian, Pautrier, Ravaut, Sézary, Clément Simon. Secrétaire général: Clément Simon. Tome V: Dermatoses en rapport avec des réactions cutanées et des troubles: Humoraux; circulatoires; endocriniens; nerveux; et de l'appareil hématopolétique. Dyschromies. Par MM. L. Chatellier, et al. Boards. Price, 300 francs. Pp. 958, with 228 illustrations. Paris: Masson & Cie, 1936.

This volume is opened by a chapter on urticaria by Flandin, Poumeau, Delille and Soulié. A general discussion of the etiology, diagnosis and treatment is well covered in the thirty-five pages devoted to the subject. This is followed by a chapter on eczema by Sézary and Horowitz. In the 108 pages the authors set forth the clinical manifestations, the histopathology, the etiology and the treatment of eczema. The chapter is too inclusive. Many of the subjects included might well be given separate treatment under special headings. Thus the photographs on pages 47, 48, 49, 58 and 69 apparently are of cases of infectious follicular dermatitis. "Eczema streptococcique" is not eczema in the American understanding of the term and "eczema du sein" might well be impetigo secondary to scabies. In other words this chapter could be broken down into many different and specific types of dermatitis. Much the same may be said of the chapter on dyshidrosis by Sézary and Miget. This is followed by a lengthy and scholarly article on pruritus and the prurigos by Léon Hunt. The whole subject is so well covered that it will serve for some time to come as a reference work. Huet makes a fundamental distinction between the primary pruriginous dermatoses and the prurigos by the presence of papules in the course of evolution in the latter. The author believes that a given agent may excite in the same tissue but in different areas papules having different clinical and even anatomic appearances. He closes by stating "Nevertheless, a large part of the pruritic dermatoses, both pure and lichenified, seem to depend, first of all, on a mental factor, the importance of which merits special attention." Excellent articles follow by Nicolas and his associates on the circulatory disturbances of the blood and lymph systems. Favre contributes an especially interesting chapter on angiodermite pigmentée et purpurique. In collaboration with Josserand, ulcus cruris is exhaustively discussed. Ferrand contributes an excellent chapter on purpura. The literature is well covered and brought down to date. Chatellier covers successfully in a few pages purpura annularis of Majocchi and Shamberg's disease. Lacapère, who died before the work was published, discusses elephantiasis and lymphangiectasies. One of the most valuable contributions to the volume is that of Nanta on the lymphoblastomas. The whole subject is so well covered and the bibliography is so complete that nothing is left to be desired. Spillmann takes up the subject of the dermatoses due to endocrine and nutritional disturbances. The twenty-six pages devoted to scleroderma are particularly instructive. He also discusses the cutaneous manifestations of thyroid disturbances, Dercum's disease, kraurosis vulvae and ulcus vulvae simplex chronicum. A short chapter on xanthoma and gout is contributed by Watrin. Simon discusses at great length the dermatoses in connection with disturbances of the nervous system. All phases of the subject, such as disturbances of sensation, trophic disturbances, acrodynia, trophedema, mal perforant, hemiatrophia facialis, ainhum and Morvan's disease, are set forth. The mental and psychopathic dermatoses are also well covered. Sézary contributes a long and scholarly chapter on the dyschromias. In collaboration with Duruy, Sézary closes the volume with a chapter on ephelides, lentigo, chloasma, dermatose pigmentée peribuccale and vitiligo.

Recent Advances in Pulmonary Tuberculosis. By L. S. T. Burrell, M.A., M.D., F.R.C.P., Senior Physician to Royal Free Hospital, London. Third edition. Cloth. Price, $5. Pp. 320, with 70 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1937.

The first chapter is devoted to immunity and infectivity. The author discusses the attack of leukocytes on the tubercle bacilli when they first enter the body and points out that an initial infection does not protect the body against a subsequent excessive dose. He states further that with tuberculosis there can be no question of getting an immunity from a first infection in any way comparable to that obtained by smallpox, mumps or scarlet fever. He says that allergy may itself be a danger but that a primary infection proceeding to an acute and general tuberculosis is extremely rare. In the chapter on prevention the author calls attention to the fact that the word cure should rarely be used in connection with tuberculosis, since many patients leave the sanatorium in excellent health and yet experience shows that they are much more likely to develop progressive disease during the next few years than the ordinary individual. The Grancher system of protecting children against infection is discussed and the various methods of immunization that have been attempted are presented. Under the subject of BCG, attention is called to the Lübeck disaster, to a series of deaths following the administration of BCG in Hungary, and to another series in Chile, where four of ten vaccinated children developed clinical tuberculosis. Burrell is of the opinion that BCG produces relative immunity for a time, although not sufficient to do more than delay the spread of the disease and increase by a short time the life of the infected animal. He is of the opinion that it is a wise procedure to desensitize persons who are hypersensitive to tuberculoprotein. In the chapter on diagnosis the usual symptoms, physical signs and laboratory procedures are discussed. The tuberculin test is presented at some length. Blood examination, such as the sedimentation test and differential leukocyte counts, are given their proper place in the examination. He states that one common source of failure to interpret x-ray appearances is the attempt to draw conclusions from a film alone. He is a firm believer in the use of the fluoroscope. A long chapter

is devoted to prognosis, another to complications and their treatment. The subject of tuberculosis in children and bovine tuberculosis is discussed and he calls attention to the fact that, in England, 40 per cent of the cows react positively to the tuberculin test and 6.5 per cent of raw market milk contains live tubercle bacilli. Moreover, 23.3 per cent of the cases of extrapulmonary tuberculosis in human beings is due to the bovine type of tubercle bacillus. The last 173 pages are devoted to treatment. One chapter deals with general treatment, in which such factors as rest are discussed; another to medicinal treatment, in which the various drugs and vitamins are presented. All forms of collapse therapy are discussed in the last two chapters. The book contains twenty-two illustrations in the text, and there are forty-eight located at the end of the book. These consist of illustrations made from x-ray films of the chests of persons, ranging from those of normal chests to those with various stages of disease. Collapse therapy is beautifully illustrated. This book is well worth a place in the library of every physician who desires to augment his information on tuberculosis.

Handbuch der Biochemie des Menschen und der Tiere. Herausgegeben von Prof. Dr. phil. et med. Carl Oppenheimer. Ergänzungswerk. Band III. Second edition. Paper. Price, 84 marks. Pp. 1,162, with 30 illustrations. Jena: Gustav Fischer, 1936.

Metabolism in birds, cold-blooded animals and invertebrates is first reviewed; second, specific metabolism in various biologic phenomena such as growth, pregnancy, muscular work; third, metabolism in pathologic conditions; fourth, metabolism in specific organs, and, fifth, the metabolism of specific food constituents. In the first group Gürsching emphasizes temperature regulation, basal metabolic rate and relation of body surface area thereto, also starvation effects and specific dynamic action in birds and cold-blooded animals. Paul Krüger discusses the general composition and metabolism in invertebrates and frequently in various stages of metamorphosis. Under the second subdivision Hans Aron and Karl Klinke give an extensive survey on the biochemistry of growth, Zuntz on the exchange of various tissue constituents between mother and offspring, Gunther Lehmann on metabolism during hard muscular work, Theodor Brugsch on metabolism during starvation and undernutrition, T. A. Maass on the effect of climate, and Pincussen on the effect of various radiations on the metabolism in the organism and various tissues. In pathologic conditions Max Reiss reviews the general and specific phases of metabolism as related to the thyroid, pituitary, adrenals and gonads. Maass reviews metabolism in hyperthermia, Peritz in nervous disorders, Aron and Klinke in deficiency diseases, and Zuntz metabolism as related to menstruation and pregnancy in women. The specific metabolism of individual tissues is presented by Karl Lohmann on muscle, heart (with Weicker), glands and endocrines, by Steindorff on the eye and by Gottschalk on tumor tissue. The metabolism of specific food constituents is reviewed by Klinke on water and minerals, by Joachim Kühnau on carbohydrates, fats, phospholipins, glycolipins and sterols, by Kurt Felix on proteins, by Adolph Gottschalk on abnormal protein metabolism, by Otto Fürth on creatine and creatinine and by Flössner on nucleic acid. The regulation mechanism, the second main division, is subdivided under the titles of nonendocrine and endocrine and vitamin regulations. The nonendocrine control is reviewed by Erich Grafe on nerve regulation of metabolism, Klothilde Gollwitzer-Meier on regulation of respiration, Josef Kapfhammer on liver in metabolism, and Heinrich Gerhartz on organs involved in blood formation and iron metabolism. Endocrine regulations are covered in the main by Max Reiss on the thyroid, adrenals, thymus, gonads, pituitary and parathyroid with Westphal emphasizing the chemistry of the sex hormones, Joachim von Ledebur reviewing the endocrine function of the pancreas and Werle the organ specific substances active in the circulation. In the last mentioned section the numerous pressor and depressor substances which have been detected by physiologic methods in various tissues and body fluids are considered. Vitamin regulation is presented by Brockmann on vitamin A, Rudy on the flavines, Heinz Ohle on cevitamic acid, Henry Albers on vitamin and plant growth stimulants, and Aron and Klinke on biology of vitamins, their quantitative estimation, distribution and need. This addition to the well known treatise in biochemistry is of the same high standard in organization and completeness as the previous volumes. In view of the variety of views expressed in different chapters it is not surprising that one finds considerable duplication. This is not, however, a serious fault.

The Hoover Policies. By Ray Lyman Wilbur, President of Stanford University, and Arthur Mastick Hyde. Cloth. Price, $3. Pp. 667. New York: Charles Scribner's Sons, 1937.

Controversialists for many years to come will use this volume as a source book of facts and arguments. The major portion of the space is devoted to a description of the policies and activities set in motion by Herbert Hoover as Secretary of Commerce and as President. These include commissions of investigation, cooperatives, protection of children, expansion of public health activities, housing, prison reform, old age pensions, unemployment insurance and "diffusion of property ownership." Hoover urged the child labor amendment, conducted an extensive investigation on waste in industry, set up machinery for collective bargaining, established the Farm Board, suggested organized planning of land use, vetoed the bonus, created machinery for the control of the radio, proposed an elaborate system of planning of flood, navigation and power works, created a new banking policy, established the Reconstruction Finance Corporation and recommended stock exchange regulation. He advocated "government-regulated business, which I believe is the American system" as contrasted with "unregulated business" or "government-dictated business." He urged the reorganization of the federal administration in the interest of efficiency, adopted special measures for the relief of those injured by drought, denounced monopoly and looked to relief by encouraging competition, and "was probably the original exponent of enlarging government programs of public works and private programs of construction as relief to unemployment in time of business depression."

Having listed this remarkable record of achievement, the tone of the book changes with the election of 1932 and becomes a criticism of the policies and measures used by the succeeding administration. The thesis of this section is that the downward swing of the depression had ended early in 1932 and that recovery was already under way at the time of the election. The conclusion is drawn that the depression from then on was due largely to the actions of the succeeding administration. This argument is supported by numerous addresses given by former President Hoover during this period. The editors have succeeded in putting together the writings and addresses with little additional matter in such a way as to make an interesting and informative, if partisan, history of the period covered.

Nouvelle pratique dermatologique. Publiée par MM. Darier, Sabouraud, Gougerot, Milian, Pautrier, Ravaut, Sézary, Clément Simon. Secrétaire général: Clément Simon. Tome IV: Dermatoses microbiennes (fin). Dermatoses dues à des virus. Dermatoses artificielles. Par P. Blum, et al. Boards. Price, 300 francs. Pp. 964, with 333 illustrations. Paris: Masson & Cie, 1936.

The volume is opened by a short article on cutaneous gangrene by Emery. This is followed by 128 pages devoted to a discussion by Milian of the subject of cutaneous infections and streptococcic infections in detail. Tribute is due to the work of Sabouraud, so ably supported by Milian, on the cutaneous manifestations of the streptococcic infections of the skin. It is unfortunate that American writers do not differentiate clearly between the streptococcic dermatoses and the staphylococcic dermatoses. If one desires to have a clear conception of the differences, one has only to read the article by Milian and the one by Sabouraud on folliculitis. Between the two is an excellent dissertation on the cutaneous complications of gonorrhea, by Perin. The same author gives a description of the lesion known in the French literature as botryomycome but which is generally recognized now as granuloma pyogenicum or telangiectaticum. Ulcus vulvae acutum is set forth by Roederer and Lanzenberg. An excellent chapter is that of Ravaut and Ferrand on the virus dermatoses. This includes the verrucae, vegetations, molluscum contagiosum, herpes and zona. Gastinel contributes a long and masterly chapter on the eruptive fevers. Pemphigus is treated in an authoritative manner as only Hudelo would treat it. Inguinal lymphogranulomatosis

is described in detail by Nicolas and Favre, who originally gave to the world the description of this comparatively new and now important dermatosis. Pityriasis rosea is thoroughly discussed by Gougerot. Milian is allotted 212 pages for an exposition of the artificial dermatoses resulting from the action of the chemical, physical and mechanical agents. Every phase of the subject is thoroughly covered. Chatellier gives an excellent description of the dermatoses due to thermal changes. Radiodermatitis is discussed at length by Laborde. The volume is closed by an interesting and stimulating discussion of the effects of light on the skin by Jausion.

Syphilis: The Next Great Plague to Go. By Morris Fishbein, M.D., Editor, Journal of the American Medical Association and of Hygeia, the Health Magazine. Cloth. Price, $1. Pp. 70, with 11 illustrations. Philadelphia: David McKay Company, 1937.

Dr. Fishbein has written a booklet that contains a tremendous amount of factual data. He believes that with proper utilization of the knowledge now at hand it would be possible to stamp out the disease entirely. "Whether or not this result will be accomplished depends on the extent to which the people are willing to cooperate with their doctors and health departments." After a brief historical review of the discovery of the causal spirochete he discusses the progress against syphilis, emphasizing the importance of the Wassermann test, the examination of the spinal fluid and the discovery of the arsphenamines, also touching on the experimental work of culture and transmission of the disease to the lower animals. The third chapter, on the prevention of syphilis in the prospective mother and in the child, is important and contains nformation which unfortunately is often not possessed by the general practitioner and other physicians concerned with obstetrics and the care of the new-born. The charts and illustrations are well chosen, and due acknowledgments are made to the various sources from which they have been selected. This simple, straightforward booklet should have a wide acceptance by the public as well as by the medical profession.

Die Leberkrankheiten: Allgemeine und spezielle Pathologie und Therapie der Leber. Von Prof. Dr. Hans Eppinger, Vorstand der I. Medizinischen Universitätsklinik in Wien. Paper. Price, 66 marks. Pp. 801, with 111 illustrations. Vienna: Julius Springer, 1937.

The author is too well known to require any statement as to his ability and experience. His researches on the reticuloendothelial system, its importance in the elaboration of bile from red blood corpuscles, and the role of the spleen in many diseases of the liver are well known to all. In this rather large volume are collected an enormous amount of material from the literature and a considerable amount from American investigators and from the author's own experimental and clinical work. One can find not alone the various tests of liver function but also an explanation of the modus operandi and an evaluation of the test. It is impossible to elaborate on a review of this book in its entirety because the subject matter as presented is too large. The clinical discussions are as worthy of study as are the theoretical ones. It is not necessary to say that the experimental side would be interesting to the research worker. The book is well illustrated and has a large bibliography, with direct references to the topic under discussion. There are many well executed illustrations. This book recommends itself to the clinician and the research worker.

A Textbook of Histology. By Harvey Ernest Jordan, A.M., Ph.D., Professor of Histology and Embryology, University of Virginia. Seventh edition. Cloth. Price, $7.50. Pp. 738, with 610 illustrations. New York & London: D. Appleton-Century Company, Incorporated, 1937.

The first edition of Jordan's textbook, which appeared in 1916 with Jordan and Ferguson as joint authors, was itself the successor to "Normal Histology and Microscopical Anatomy," by Jeremiah S. Ferguson. The seventh edition differs from the sixth in form; the pages are larger and there are 738 instead of the 857 in the sixth edition. Thirty-nine of the 610 illustrations have been replaced by new ones, of which about half have been furnished by Prof. Irving Hardesty of Tulane University. Brief additions deal with recent ideas of functional activity. In the article on bone formation the views of Macewen, Policard and Leriche are summarized; according to them the periosteum and the osteoblasts have no osteogenic significance—bone formation and resorption are induced by humoral rather than by cellular factors. Osteoblasts, and especially osteoclasts, are osteolytic in function. Other textual additions deal with the endocrine glands. The hormones reported by Allen and Hisaw which supplement the effect of theelin are described. Swingle's view that the cortex of the adrenal produces hormones which regulate the volume of blood and Britton's view that it is concerned also with the maintenance of carbohydrate balance are presented. Rowntree's interesting experiments on the thymus and pineal functions, cumulative through several generations, are reported, that of the thymus promoting early development and that of the pineal retarding growth but accelerating differentiation (precocious dwarfism).

Physiologie générale des articulations à l'état normal et pathologique. Par A. Policard, professeur à la Faculté de médecine de Lyon. Paper. Price, 36 francs. Pp. 214, with 25 illustrations. Paris: Masson & Cie, 1936.

The subject is divided into seven parts: (1) joint cartilage; (2) the fibrocartilaginous appearance next to the joint surface, that is to say, cushion-swelling-pad-cap, the marginal bourrelets and the menisci; (3) the synovial lining of the joint cavity; (4) the joint cavity and the synovia which lubricates it; (5) the fibrous deposits of the joint, i. e., in the capsule and its ligaments; (6) the innervation of the joint, and (7) the periarticular connective tissue. The author describes an ingenious apparatus called the elastometer, which he uses to determine the elasticity of the joint cartilage. The value of the manuscript is enhanced by some fine microscopic, histologic and schematic representations.

Incunabula in the Huntington Library. Compiled by Herman Ralph Mead. Cloth. Price, $7.50. Pp. 386. San Marino, California, 1937.

As usually defined, incunabula are the first printed books, those issued between the time of the origin of printing, roughly 1450, to the end of the century, 1500. Nearly all the early masters of typography issued medical works. Osler's bibliography of incunabula medica, which limits itself to the dates 1467-1480, lists 208 items. The Huntington Library has long been known to have one of the most magnificent assemblages of these books in the world. In 1931 Mr. Mead published a list of the "Incunabula Medica" there, which supplied the needs of the medical bibliographer. It ranks with the catalogue of incunabula of the Boston Medical Library and the College of Physicians of Philadelphia. For general categories of medical incunabula, the research worker has Stockton-Hough, Osler and the recently published short title list of scientific and medical incunabula by Arnold Klebs. The catalogue of all the incunabula at the Huntington Library just completed lists 5,291 items. It follows the arrangement of Proctor's index of the British Museum and Bodleian. The items are grouped under country, then the city in the country, and then the printer in that city: under each heading the arrangement is chronological. Two indexes, one of authors and titles and one of printers and places, occupy the last 150 pages of this valuable bibliography.

An Introduction to the Social Studies: An Elementary Textbook for Professional and Preparatory Groups. By Joseph K. Hart, Ph.D., Associate in Educational Sociology, Teachers College, Columbia University. Cloth. Price, $2. Pp. 203. New York: Macmillan Company, 1937.

The evolution from groups to communities, from family to institutions and from primitive society to modern cities is briefly sketched. "In one sense, we can say that the whole history of the race is a history of invention and discovery." Invention is the disturbing element in social organization and compels continuous changes in social institutions. The lag between the practical application of inventions and the adjustment of social institutions to the necessary changes creates "social problems." This work, which is clearly intended for a textbook in secondary schools, postulates a great number of problems and seeks to encourage the student to work out his own solutions. The only exception is in the chapter on our social professions, where, perhaps, the author is least capable of giving dogmatic solutions and where alone he does occasionally seem to assume that the problem of medical service leads to a conclusion that "we do know that skill and service must be completely socialized, in some way."

Unemployment Relief in Pennsylvania, January 1, 1936-December 31, 1936. Fourth Annual Report of the Executive Director, State Emergency Relief Board. Paper. Pp. 22. Harrisburg, Pennsylvania: State Emergency Relief Administration, 1937.

"In the fall of 1936 the State Emergency Relief Administration improved both its service to the unemployed and its efficiency of operation by establishing cash relief in the sixty-five counties which had previously granted direct relief in the form of commodity orders." By enabling families to choose the source from which they would purchase goods and to budget their own needs, cash relief has made for economy and greater efficiency and has also made it possible to simplify the method of determining eligibility and the amount of relief to be granted. Also, it is largely responsible for a decline of 61.3 per cent in the administrative personnel, while the case load decreased 39.5 per cent. The number of persons receiving relief decreased from an average of 1,636,000 in 1935 to 1,456,000 in 1936.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Release of Original Tortfeasor Releases Physician Whose Negligence Aggravates Injury.—The plaintiff sustained a fracture of the neck of his right femur as a result of being hit by an automobile. The defendant in the present action attended him. After the accident, the plaintiff sued the driver of the automobile and the suit was eventually settled out of court. The plaintiff gave the driver a written release from liability for all claims arising out of the accident. About a year later the plaintiff sued the defendant, asserting that he, the defendant, carelessly and improperly treated the fracture, with resulting injury. The trial court directed a verdict for the defendant and, after judgment on the verdict was entered, the plaintiff appealed to the Supreme Court of Pennsylvania.

The general rule is, said the Supreme Court, that there can be no recovery in a suit against a physician for negligent aggravation of injuries after a settlement has been effected with the tortfeasor who caused the accident. In the action against the driver, the plaintiff's recovery for the injury to his hip would have included the added injury caused by the alleged negligence of the defendant. Physicians, being human, said the court, are apt occasionally to lapse from prescribed standards, and the likelihood of carelessness, lack of judgment or of skill, on the part of a physician employed to effect a cure for a condition caused by another's action, is therefore considered in law as an incident of the original injury. If the injured person has used ordinary care in the selection of a physician, any additional harm resulting from the latter's mistake or negligence is considered as one of the elements of the damages for which the original wrongdoer is liable.

For the final condition of his hip, the plaintiff could have sued, and did sue, the driver of the automobile; for the aggravation of the original condition, the plaintiff could have sued, and did sue, the defendant who treated him. He could have pursued both actions to judgment. For the same injury, however, an injured party can have but one satisfaction and the receipt of such satisfaction, either as payment of a judgment recovered or consideration for a release executed by him, from a person liable for such injury necessarily works a release of all others liable for the same injury and prevents any further proceeding against them. This is true, the court pointed out, even though it was intended, or the release expressly stipulated, that the other wrongdoers should not thereby be released. Nor is it material whether the tortfeasors involved committed a joint tort or concurrent or successive torts, because the principle which underlies the rule is that the injured person is given a legal remedy only to obtain compensation for the injury done to him, and when that compensation has been received from any of the wrongdoers, his right to further remedy is at an end. If a tortfeasor is liable for only a part of the damage, and another tortfeasor only for another part, a release of one does not, of course, release the other; but where the two are liable for the same damage, no matter on what theory their respective liabilities are predicated, the rule applies.

Since in the present case the plaintiff was compensated, by a settlement with the driver of the automobile, for all injuries, both those originally and those ultimately arising out of the accident, including the aggravation of the hip condition by the defendant's alleged negligence, he cannot obtain from the defendant a second satisfaction. The judgment of the trial court for the defendant was therefore affirmed.—*Thompson v. Fox (Pa.), 192 A. 107.*

Workmen's Compensation Acts: Trophic Ulcers in Relation to Diabetes, Arteriosclerosis and Trauma.—The claimant, 72 years of age, was employed by the defendant Goodwill Industries to repair toys, his employment requiring him to stand on his feet during most of the hours of work. During the period of his employment and for some time prior thereto he had suffered from arteriosclerosis of his lower extremities and from diabetes. This combination of ailments resulted in impairment of the circulation of blood in his feet, and he had had trouble with his feet. Shortly before he was compelled to leave the employment, "the bottom of his feet near the toes broke open," and he was unable to walk thereafter. This condition was diagnosed as trophic ulcers of both feet. The industrial commission found that the claimant's condition probably would have resulted from his physical infirmities irrespective of his standing position at work and dismissed his claim for compensation. The claimant thereupon brought suit to review the order of the commission and, from a judgment confirming that order, he appealed to the Supreme Court of Wisconsin.

There was no relation, said the Supreme Court, between the claimant's employment and his diabetes and arteriosclerosis. The record failed to disclose any event that constituted an accident. The evidence merely showed that the claimant ultimately broke down while employed and that the ordinary physical wear and tear of his work may have had some slight tendency to accelerate his disability. A mere breakdown due to disease is not compensable even if the physical effort involved in the work made some contribution to the final disability. The commission correctly found that the claimant was not suffering from an occupational disease and that he had not sustained an accidental injury. The judgment upholding the order of the industrial commission denying compensation was affirmed.—*Schmitt v. Industrial Commission et al. (Wis.), 272 N. W. 486.*

Workmen's Compensation Acts: Dissecting Aneurysm of Aorta and Its Rupture in Relation to Trauma.—Nicholes was 30 years of age and in good health. In the course of his employment he assisted the operator of a caterpillar tractor, the tractor being used to push over and uproot trees and shove them and rocks to one side in grading and leveling an uneven and rough terrain. Nicholes was therefore subjected to considerable jolting and jarring. On finishing work, July 2, Nicholes was excessively tired and his abdomen pained him. When he returned home from work on July 3, on which day he had driven the tractor all day, he was still excessively weary and complained of pains in his chest and left arm. That night he died before medical aid arrived. The industrial commission entered an award in favor of the widow, and the employer brought an original certiorari proceeding in the Supreme Court of Utah to review that award.

An autopsy disclosed two tears in the intima, or inner lining, of the thoracic portion of the aorta which had permitted blood to escape into the wall of the vessel and dissect its coats so that a dissecting aneurysm was formed. The aneurysm had dissected toward the heart as far as the junction of that organ with the aorta, where it ruptured and permitted blood to escape into the pericardial sac, causing what is known as a hemopericardium. Tiredness and fatigue or weariness may not of themselves be evidence of an accident or an accidental injury, said the Supreme Court, but in a normally healthy person pursuing an occupation in which normally healthy persons do not become tired or weary those things may be and frequently are symptoms of an unusual condition or a weakness, which when

properly interpreted on the basis of a subsequent examination may point quite unerringly to a cause which will bring the case within the terms of an accident arising out of or in the course of the employment. There was ample evidence, said the court, that in the operation of the tractor there was considerable jolting and jarring. There was further evidence, based on a physical examination which the employer required of Nicholes before employing him, that at the time of the employment the workman was in good physical condition. All medical witnesses before the commission agreed that such a rupture as occurred in this case can be caused either by disease, emotional stress, physical exertion or jolting and jarring. The physician who performed the autopsy and another medical witness testified that an examination of the heart indicated it to be normal except that an imprint on it evidenced a "mild carditis" of the rheumatic type which had healed years before and could not have caused the rupture. In their opinion the rupture and the dissecting aneurysm were the cause of death, and the jarring and jolting of the tractor not only could but did cause the rupture. Two physicians, called by the employer, designated certain spots on the workman's aorta as atheromatous plaques which, they testified, was a condition that could cause the rupture. All the medical witnesses agreed that the aneurysm was of recent origin, varying their estimates from a matter of hours to a maximum of ten days.

In view of this testimony, the Supreme Court was of the opinion that the industrial commission was warranted in entering an award for the widow. The award was therefore affirmed. —*Columbia Steel Co. v. Industrial Commission et al. (Utah), 66 P. (2d) 124.*

Compensation of Physicians: When Fees of Medical Witnesses Taxable as Costs.—By statute in Louisiana the fees and expenses of expert witnesses may be taxed as court costs. Under that act, said the court of appeal of Louisiana, Orleans, fees paid a medical witness who testifies with respect to facts learned by him prior to the occurrences out of which the litigation resulted may not be taxed as costs, since the witness does not testify as an expert witness but rather as an ordinary witness. If such a witness is called on to express an opinion as an expert, in addition to giving factual testimony, the fee paid for the opinion testimony only may be taxed as costs. If a physician, in addition to testifying as an expert witness, assists counsel at trial in the cross-examination of adverse witnesses, the part of the fee paid to such a witness that is fairly attributable to the services rendered counsel is not taxable as costs.—*Cutitto v. Metropolitan Life Ins. Co. (La.), 172 So. 812.*

Workmen's Compensation Acts: Psychosis Following Bilateral Herniotomy and Appendectomy.—The claimant, Dehron, sustained a right inguinal hernia as a result of his employment. During the course of an operation to repair that hernia, an incipient left inguinal hernia was repaired and the claimant's appendix was removed. Prior to this time the claimant's mental condition was normal. Shortly thereafter he developed symptoms of psychosis, which eventually necessitated his confinement in a sanatorium. The compensation commission awarded him compensation under the workmen's compensation act for the psychosis, finding that that condition resulted from the operation to repair the industrial hernia. The employer appealed to the superior court, Fairfield County, Conn., which affirmed the award and the case eventually reached the Supreme Court of Errors of Connecticut.

The only question before the court was whether the evidence justified the compensation commission in finding that the operation for the industrial hernia caused the claimant's psychosis. The causal relation between that operation and the psychosis, said the court, could be established only by expert testimony. The only medical expert testifying with respect to this matter stated that the three operations combined produced the psychosis and that he could not tell which of the three operations caused it or how to separate the effect of any one. To attempt to do so, in his opinion, would be mere speculation. For the commission to conclude from this testimony, said the court, that the operation for the industrial hernia caused the psychosis was a mere guess, conjecture or surmise and was entirely unwarranted by any legally sufficient evidence.

The court believed, however, that the fullest opportunity should be given the claimant to develop further facts in evidence before the compensation commissioner and remanded the proceedings. In doing so, the court said that by analogy to the law of torts the principle determinative of the defendant's liability is that when an employer is liable to compensate for an injury he is also liable for any additional bodily harm resulting from acts done by third persons in rendering aid which the injury reasonably requires. With respect to medical and surgical treatment, the employer is liable for additional injuries which result from the risks normally recognized as inherent in the necessity of submitting to such treatment and not for harm caused by misconduct which is extraordinary and therefore outside such risks. On further hearing before the commission, the court said, the question would be: Did the two operations, aside from the one to repair the industrial hernia, fall within the rule? As a practical proposition, the court pointed out, the determination of that question would depend on whether or not a surgeon, exercising that care, skill and diligence which surgeons in the general neighborhood of the town in which the operations were performed possessed and utilized in like cases, confronted with the situation that was present in this case, would perform all three operations as inherent in a proper treatment for the original compensable injury.—*Dehron v. Clark (Conn.), 191 A. 526.*

Workmen's Compensation Acts: Refusal to Undergo Operation.—The claimant, in the course of his employment in 1932, sustained an injury to his back that resulted in total disability. He was paid compensation under the West Virginia workmen's compensation act until August 1935, when further compensation was denied because of his refusal to submit to an operative fusion of the lumbosacral and sacral joints. He thereupon appealed to the Supreme Court of Appeals of West Virginia.

The contemplated operation, said the Supreme Court of Appeals, was not described in the record nor was its attendant suffering mentioned. Four physicians recommended it, one of whom testified that the operation was a reasonably safe one, that the claimant was in good general physical condition and that he would be relieved of disability by the operation. Five other physicians opposed the operation, differing with the other physicians in the case with respect to their diagnosis. With such sharp divergence of professional opinion, the court said, the claimant's refusal to submit to the operation was not unreasonable. An operation may be made the condition of further compensation only when surgical opinion is substantially in accord that the operation is indicated, that it is reasonably safe and not attended by unusual suffering, that it will likely produce material physical improvement, and that it is one which a person of ordinary prudence and courage would undergo for his own betterment, regardless of compensation. The Supreme Court of Appeals therefore reversed the ruling denying further compensation and remanded the case for further consideration, uninfluenced by the claimant's refusal to submit to the proposed operation.—*Gillam v. Workmen's Compensation Appeal Board (W. Va.), 191 S. E. 204.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Los Angeles, Jan. 16-20. Dr. Carl E. Badgley, 1313 East Ann St., Ann Arbor, Mich., Secretary.

American Orthopsychiatric Association, Chicago, Feb. 24-26. Dr. Norvelle C. La Mar, 210 East 68th St., New York, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 14-15. Dr. W. D. Cutter, 535 North Dearborn St., Chicago, Secretary.

Middle Section, American Laryngological, Rhinological and Otological Society, St. Louis, Jan. 26. Dr. James B. Costen, Beaumont Bldg., St. Louis, Chairman.

Pacific Coast Surgical Association, Los Angeles, Feb. 22-25. Dr. H. Glenn Bell, University of California Hospital, San Francisco, Secretary.

Southern Section, American Laryngological, Rhinological and Otological Society, Atlanta, Ga., Jan. 24. Dr. Murdock S. Equen, 144 Ponce de Leon Ave. N.E., Atlanta, Ga., Chairman.

Western Section, American Laryngological, Rhinological and Otological Society, Santa Barbara, Calif., Jan. 29-30. Dr. Arthur C. Jones, Eastman Bldg., Boise, Idaho, Chairman.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1927 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

14: 515-642 (Nov.) 1937

Acute and Chronic Compression of the Heart. C. S. Beck, Cleveland. —p. 515.

*Use of Mercupurin in Treatment of Congestive Heart Failure and in Mobilization of Excess Body Fluid. H. J. Stewart and C. H. Wheeler, New York.—p. 526.

Extracardiac Determinants of Site and Radiation of Pain in Angina Pectoris, with Especial Reference to Shoulder Pain. E. P. Boas and H. Levy, New York.—p. 540.

Sixteen Years' Experience with Heart Disease in Pregnant Women. B. E. Hamilton, Boston.—p. 555.

Organic and Relative Insufficiency of Pulmonary Valve. J. McGuire and R. J. McNamara, Cincinnati.—p. 562.

Unusual Case of Auricular Parasystole Showing "Exit" Block. L. N. Katz, J. L. Eschelbacher and S. Strauss, in collaboration with S. H. Robertson and H. Binswanger, Chicago.—p. 571.

Electrical Axis in Simultaneous Leads: I. Factors Increasing Dispersion of Normal Values. R. C. Robb and Jane Sands Robb, Syracuse, N. Y.—p. 588.

The Symballophone: Modified Stethoscope for Lateralization and Comparison of Sounds. W. J. Kerr, T. L. Althausen, A. M. Bassett and M. J. Goldman, San Francisco.—p. 594.

*Quantitative Study of Cutaneous Capillaries in Hyperthyroidism. E. Roberts and J. Q. Griffith Jr., Philadelphia.—p. 598.

Treatment of Scleroderma by Means of Acetyl-Beta-Methylcholine Chloride (Mecholyl) Iontophoresis. A. W. Duryee and I. S. Wright, New York.—p. 603.

Fainting Attacks Resulting from Hypersensitive Carotid Sinus Reflexes. H. L. Smith, Rochester, Minn.—p. 614.

Use of Quinidine Sulfate Intravenously in Ventricular Tachycardia. J. Hepburn and H. E. Rykert, Toronto.—p. 620.

Mercupurin in Treatment of Heart Failure.—Stewart and Wheeler have observed the effects of mercupurin in patients for one year and have given 438 injections of this mercurial diuretic to sixty-six patients who presented physical signs of excess fluid in the tissues. Fifty-two patients suffered from heart failure of the congestive type, nine from cirrhosis of the liver exhibiting ascites, two from the nephrotic stage of chronic glomerular nephritis, one from hydrothorax and ascites of unknown etiology, one from tuberculosis of the peritoneum exhibiting ascites and one from carcinomatosis of the pleura and peritoneum with hydrothorax and ascites. Each patient received from one to forty-five injections; 2 cc. was the dose usually given. It is their impression that mercupurin is at least equal and possibly superior to salyrgan in its diuretic effect. The diuretic effect varied between 200 and 5,900 cc. but was most commonly between 1,000 and 2,000 cc. Analyzed in another fashion, the urinary output was increased as much as nineteen times, but most frequently the increase did not exceed five times. It appears to be equally effective irrespective of the etiologic type of heart disease; the magnitude of the diuresis appeared to be roughly proportional to the amount of excess fluid stored within the tissues; ammonium chloride appears to enhance its diuretic effect; diuresis in patients suffering from cirrhosis of the liver exhibiting ascites appears to be less striking, although the drug was frequently effective in preventing the recurrence of ascites; good results were obtained consistently in patients suffering from chronic constrictive pericarditis. Effects that might have been construed as toxic occurred in only three patients. Thrombosis or slough did not occur at the site of injection. Of the known mercurial diuretics, mercupurin is to be preferred when it is desired to mobilize fluid.

Cutaneous Capillaries in Hyperthyroidism.—Roberts and Griffith observed the capillary counts in an area of approximately 2 sq. mm. in normal controls and in hyperthyroid patients. The area chosen was the extensor surface of the forearm midway between the elbow and the wrist. Capillary counts were made in the same area before and after pricking histamine into the skin. While absolute counts in different patients cannot be compared directly, percentage increase in the same patient is considered significant. Of the sixteen hyperthyroid patients, the increase averaged 16 per cent; of the fourteen controls, 120 per cent. It is suggested that in the hyperthyroid state an increased dilatation of the cutaneous circulation assists in the loss of heat by the body. However, the degree of dilatation is not related quantitatively to the height of the basal metabolic rate.

American Journal of Clinical Pathology, Baltimore

7: 467-570 (Nov.) 1937

Opportunities of the Chemistry Division for Service to Clinical Medicine. F. W. Sunderman, Philadelphia.—p. 467.

The One-Hour Two-Dose Glucose Tolerance Test. S. E. Gould, Detroit. —p. 474.

Observations on the One-Hour Two-Dose Dextrose Tolerance Test. J. S. Sweeney, J. J. Muirhead and L. E. Allday, Dallas, Texas. —p. 482.

Control Antigen Emulsions for Microscopic Slide Precipitation Tests for Syphilis. B. S. Kline, Cleveland.—p. 490.

Hematologic Observations on Bone Marrow Obtained by Sternal Puncture. P. Vogel, L. A. Erf and N. Rosenthal, New York.—p. 498.

Congenital Neuroblastoma of the Adrenal: Sympathoblastoma, Sympathogonioma, Ganglioma Embryonale Sympatheticum or Sympathoma Embryonale. V. W. Bergstrom, Binghamton, N. Y.—p. 516.

*Etiology and Pathology of Agranulocytic Angina: Present-Day Findings and Hypotheses. T. Fitz-Hugh Jr., Philadelphia.—p. 524.

Corn Whisky and Strychnine Poisoning. J. C. Norris, Atlanta, Ga.—p. 531.

Agranulocytic Angina.—Fitz-Hugh presents the chart of a case in which recovery occurred and emphasizes that the disease (which he believes to be an entity in the same sense that pernicious anemia and bronchial asthma are entities) does not involve the red cells or platelets or the so-called coagulation factors of the blood. The pathologic changes are (1) maturation arrest of the myeloid series of leukocytes at the myeloblast-myelocyte level, (2) arrest or partial nonmigration into the blood stream of the other leukocytes, (3) maintenance of normal red cell and platelet structure and function, (4) oropharyngeal and other mucosal and cutaneous ulceration and necrosis with complete or nearly complete absence of polymorphonuclear infiltration, (5) invasion by "opportunist bacteria" with various types of ensuing sepsis and (6) recovery initiated by myelocytic hyperplasia of the bone marrow, a myelocyte crisis in the peripheral blood, sometimes a monocytosis as well, and then a return of normal polymorphonuclear and other white cells to the circulation and tissues with ensuing tissue recovery (provided some septic or necrotic process has not already gone beyond repair).

American Journal of Hygiene, Baltimore

26: 423-574 (Nov.) 1937

The Age Distribution and the Infection Rate of Yaws in Jamaica. G. M. Saunders, Kingston, Jamaica, B. W. I., and H. Muench, New York.—p. 423.

Present Status of Hookworm Infestation in North Carolina. A. E. Keller, W. S. Leathers, Nashville, Tenn., and J. C. Knox, Raleigh, N. C.—p. 437.

Prevalence and Distribution of Hookworm Infection in Egypt. J. A. Scott.—p. 455.

Observations on Transmission of Hookworm Infection in Egypt. J. A. Scott.—p. 506.

Tuberculosis Studies in Tennessee: Infection, Morbidity and Mortality in Families of Tuberculous. H. C. Stewart, R. S. Gass, Franklin, Tenn.; R. L. Gauld, Columbia, Tenn., and Ruth R. Puffer.—p. 527.

*Risk of Mortality Among Offspring of Tuberculous Parents in a Rural Area in the Nineteenth Century. J. Downes, New York.—p. 557.

Risk of Mortality Among Offspring of Tuberculous Parents.—Downes secured a history of the parents and siblings of both the husband and the wife in each of 1,400 families in the morbidity survey. The data included the date of birth of each member of the family, the age and date of death and the cause of death for all who were deceased at the time the survey was made. The records include some families in which the offspring were born previous to 1850 as well as some in which the offspring were born since 1900. The data for this particular study consist of records for 1,062 families in which all the children were born previous to 1901. In calculating the mortality experience of the population composed of persons born previous to 1901, the parents are excluded and only the offspring who survived to 1 year of age in the 1,062 families are included. Members of the tuberculous families, born in the period 1868-1897, had an average mortality from all causes

significantly higher than the mortality observed in a sample population based on the 1,062 families from which they were drawn. In the tuberculous families a considerable excess in mortality was noted at ages from 10 to 39, the ages when in rural areas tuberculosis is known to take its highest toll of life. The average tuberculosis death rate was 7.2 per thousand person-years among the offspring in families in which there was a tuberculous parent. This rate compared with the average mortality in the sample population showed that the risk of mortality from tuberculosis was nine times greater for offspring in the tuberculous families than for the general population. The mortality experience in the tuberculous families of the past century was compared with that in a similar group of families drawn from the same rural area in a more recent time period. Similar death rates from all causes and from tuberculosis for all ages combined and at specific ages were noted among the offspring in the two groups. There was some indication that the risk of mortality from tuberculosis in the general population of Cattaraugus County was less in the modern period (1916-1924) than it was from forty to sixty years ago.

American Journal of Pathology, Boston

13: 881-1036 (Nov.) 1937

The Pathogenesis of Dietary Nephritis in the Rat. E. M. Medlar and N. R. Blatherwick, with assistance of J. M. Connolly, Phoebe J. Bradshaw and Susan D. Sawyer, New York.—p. 881.

*Influence of Allergy on Development of Early Tuberculous Lesions. L. Dienes and T. B. Mallory, Boston.—p. 897.

Encephalitis and Meningitis in the Chick Embryo Following Inoculation of Chorio-Allantoic Membrane with Haemophilus Influenzae. Mae Gallavan, Nashville, Tenn.—p. 911.

Infection of Chick Embryos with Haemophilus Pertussis Reproducing Pulmonary Lesions of Whooping Cough. Mae Gallavan and E. W. Goodpasture, Nashville, Tenn.—p. 927.

Specificity of Lesion of Experimental Mumps. O. Bloch Jr., Nashville, Tenn.—p. 939.

Changes in the Teeth Following Parathyroidectomy: I. Effects of Different Periods of Survival, Fasting and Repeated Pregnancies and Lactations on Incisor of the Rat. I. Schour, S. B. Chandler and W. R. Tweedy, Chicago.—p. 945.

Changes in the Teeth Following Parathyroidectomy: II. Effect of Parathyroid Extract and Calciferol on Incisor of Rat. I. Schour, W. R. Tweedy, S. B. Chandler and M. B. Engel, Chicago.—p. 971.

Morphologic Changes in Pituitaries of Rats Resulting from Combined Thyroidectomy and Gonadectomy. Isolde T. Zeckwer, Philadelphia.—p. 985.

Silver Impregnation of Reticulum in Paraffin Sections. G. Gömöri, Budapest, Hungary.—p. 993.

Cerebral Medulloblastoma. W. M. Honeyman, New York.—p. 1003.

Allergy and the Development of Early Tuberculous Lesions.—Dienes and Mallory undertook to test the applicability to tuberculosis of the hypothesis that allergy is the primary factor in determining the character of the early histologic response to the infection in susceptible animals. If such a theory is tenable, it must be demonstrated that the granulomatous lesions are not essential to the development of the delayed type of allergy and that tuberculin sensitivity develops at least as early as the appearance of the characteristic histologic picture in the initial tuberculous lesion. The first of these points was demonstrated by Dienes in 1930. The second of the imposed conditions was tested by an analysis of the time factors governing the development of hypersensitiveness and the appearance of mononuclear infiltration, fibroblastic proliferation and other factors of the granulomatous tissue response. Not later than the fourth day, sometimes even on the third day, the reaction of the animals to tuberculin—usually more evident to tubercle bacilli themselves—is clearly different in character from that observed in uninfected animals or in the first two days after the primary infection. It is quicker, is far more intense in proportion to the dosage used and microscopically can be shown to have the predominantly mononuclear characteristic of the delayed type of hypersensitivity. Even at this early stage the animals are clearly developing generalized tuberculin sensitivity. At approximately the same time period a distinct change in the character of the primary lesion can be demonstrated. Beginning sometimes on the third and becoming well marked on the fourth day, collections of large mononuclear phagocytes begin to appear as cuffs about the blood vessels and nerves, to infiltrate the stroma first at some distance from organisms and leukocytes but gradually to condense about them to form a wall several cells thick. At about this time the connective tissue cells begin to appear swollen and hyperchromatic, and mitotic figures begin to appear in abundance in them. In another twenty-four hours collagen begins to be laid down and true encapsulation is initiated. The parallelism between the appearance of demonstrable hypersensitivity and the alteration of the character of the primary lesion are closer when the two inoculations are made into similar tissues.

American Journal of Physiology, Baltimore

120: 649-824 (Dec.) 1937. Partial Index

Relation of Hypophysis and Adrenal Cortex to Removal of Excess Glucose from Blood of Rats. L. T. Samuels, H. F. Schott and H. A. Ball, with technical assistance of M. L. Lipkis and M. Chernow, Los Angeles.—p. 649.

Effect of Atropine on Gastric Secretion and Its Relation to Gastrin Theory. J. S. Gray, Chicago.—p. 657.

Electrical Potentials of Cochlea and Auditory Nerve in Relation to Hearing. J. Guttman and S. E. Barrera, New York.—p. 666.

Relation of Amniotin to Basal Metabolism of Thyroidectomized Rat. T. C. Sherwood, T. M. Wilson and H. Boneta, Lexington, Ky.—p. 671.

Effects of Mecholyl on Gastric Secretion. J. S. Gray and A. C. Ivy, Chicago.—p. 705.

*Rapid Decompression Following Inhalation of Helium-Oxygen Mixtures Under Pressure. E. End, Milwaukee.—p. 712.

Electrolyte and Water Changes in Muscle During Atrophy. H. M. Hines and G. C. Knowlton, Iowa City.—p. 719.

Effect of Hexylresorcinol on Absorption of Insulin from Gastro-Intestinal Tract of Dogs. R. G. Daggs, W. R. Murlin and J. R. Murlin, with technical assistance of Ruth L. Tomboulian, Rochester, N. Y.—p. 744.

Acetylcholine Contracture of Denervated Muscle. G. C. Knowlton and H. M. Hines, Iowa City.—p. 757.

*Relationship Between Blood Sugar Level and Rate of Sugar Utilization, Affecting Theories of Diabetes. S. Soskin and R. Levine, Chicago.—p. 761.

Relation Between Summation and Inhibition in Spinal Reflex. S. Bernstein, New York.—p. 798.

Rapid Decompression with Helium-Oxygen Mixtures Under Pressure.—End states that to obtain data for determining decompression tables for divers breathing helium-oxygen mixtures the designers of the Craig-Nohl diving dress served as voluntary subjects for tests which appear to establish beyond question the superiority of this artificial gas mixture over ordinary air for men working under pressure. The experiments were performed in a steel recompression chamber, 18 feet long and 7 feet in diameter, divided into an inner and an outer compartment by pressure-tight doors. In it pressures up to 44 pounds per square inch are available. For these experiments two sets of rebreathing apparatus were constructed, each consisting of a spirometer, a soda-lime chamber, valves, an airtight mouthpiece and necessary tubing and connections. Helium-oxygen or helium-nitrogen-oxygen mixtures prepared beforehand were admitted to these systems from a cylinder under pressure, and oxygen was added from another cylinder at will. The subjects breathed from these systems during the entire period of each experiment. After breathing a helium-oxygen mixture under pressure, the two subjects were uneventfully decompressed in less than one twenty third of the time required when compressed air is breathed. Attention is called to several possibilities of helium-oxygen mixtures as a substitute for compressed air for men working under increased pressures. While the results serve fully to justify the author's expectations for helium-oxygen mixtures, they are reported in the hope that they will stimulate more work by others in this field. The fact that the two subjects have suffered no apparent ill effects following decompression in two minutes' time after having breathed a helium-oxygen mixture at a pressure equivalent to 90 feet of sea water of approximately one hour should not be interpreted by any one as an attempt to establish this as a safe rate of decompression under the circumstances. Such figures are, however, encouraging.

Blood Sugar Level and Rate of Sugar Utilization.—Soskin and Levine compared the relation of the blood sugar level to the utilization of sugar in normal and depancreatized dogs, respectively. It was found that the completely depancreatized dog, in the absence of insulin, can utilize dextrose at any rate of which the normal animal is capable. In both the normal and the depancreatized dog the rate of dextrose utilization depends on the height of the blood sugar level. Within a certain glycemic range, the depancreatized dog utilizes less sugar at any given blood sugar level than the normal animal at the same level; but the depancreatized dog at its usual hyperglycemic level utilizes as much sugar as the normal dog, or more, at its usual normal blood sugar level. On the foregoing

basis the two supposedly opposing theories of diabetes can be reconciled. The nonutilization theory applies only in a particular restricted sense. The overproduction theory remains as the major component of the new conception. Previous work on the comparative utilization of carbohydrate by the normal and the diabetic organism must be reconsidered with due regard to the foregoing facts.

Anatomical Record, Philadelphia

69: 389-518 (Nov.) 1937

External Genitalia in Three Female Old World Primates: Note. M. F. Ashley-Montagu, New York.—p. 389.
Preliminary Studies of Hereditary Variation in Axial Skeleton of the Rabbit. P. B. Sawin, Providence, R. I.—p. 407.
Relation of Golgi Material to Secretory Process in Basophilic Cells of Anterior Hypophysis. A. J. Gatz, Minneapolis.—p. 429.
*An Early Stage of Human Implantation. J. S. Latta and J. P. Tollman, Omaha.—p. 443.
Left Postrenal Inferior Vena Cava Without Transposition of Viscera: Case. F. J. L. Blasingame and C. H. Burge, Galveston, Texas.—p. 465.
Relationships of Epithelial Components of Pituitary Gland of Rabbit and Cat. A. B. Dawson, Boston.—p. 471.
Cyclic Changes in Lymphatic Nodules. Eleanor A. Conway, Chicago.—p. 487.

An Early Stage of Human Implantation.—Latta and Tollman state that a specimen of a uterus removed surgically from a sexually active woman sent to the laboratory for pathologic examination was found to contain an ovum in the endometrium in an early stage of development. Careful examination of the implanted tissues revealed no traces of an embryonic disk, amnion or yolk sac. Nevertheless microscopic study indicated that the tissues were well preserved and features of implantation were well shown. In view of the fact that only relatively few ova in the endometrium in such an early stage of development have been described, the authors give an account of the features presented by their specimen.

Annals of Surgery, Philadelphia

106: 961-1130 (Dec.) 1937

Surgical Follow-Up Department of the New York Hospital. B. S. Ray, New York.—p. 961.
Abscess of the Tongue. G. P. Grigsby and S. E. Kaplan, Louisville, Ky.—p. 972.
Endobronchial Probing Combined with Serial Selective Bronchography Fluoroscopically Controlled. A. Goldman and R. Adams, San Francisco.—p. 976.
*A Suggested Method for More Rapidly Curing Empyema. H. Koster, L. P. Kasman and J. Rosenblum, Brooklyn.—p. 992.
Treatment of Empyema. C. I. Allen, Detroit.—p. 1005.
Carcinoma of the Ampulla of Vater. W. A. Cooper, New York.—p. 1009.
Mortality Factors in Appendicitis with Perforation. H. P. Totten, Los Angeles.—p. 1035.
Squamous Cell Carcinoma of Lower Rectum and Anus. E. L. Keyes, St. Louis.—p. 1046.
Rupture of Supraspinatus Tendon. T. W. Davis and J. E. Sullivan, New York.—p. 1059.
*Plasma Exudation: Loss of Plasma-like Fluid in Various Conditions Resembling Surgical Shock: Experimental Study. H. N. Harkins and P. H. Harmon, Chicago.—p. 1070.
Wound Healing and Neoplasia: Experimental Investigation. A. Brunschwig, D. Tschetter and A. D. Bissell, Chicago.—p. 1084.
New Method of Preparing Nonpyrogenic Intravenous Infusion Fluids: Based on Removal of Pyrogen by Adsorptive Filtration. Co-Tui, K. L. McCloskey, M. Schrift and A. L. Yates, New York.—p. 1089.

Method for Treatment of Empyema.—From 1929 to 1934 Koster and his associates treated 118 cases of empyema by open drainage involving rib resection. The patients were operated on under spinal anesthesia and a segment of rib was removed, so that the resulting opening was large enough to admit inspection and digital examination immediately after the cavity was thoroughly emptied by suction. A drainage tube was placed in the cavity and the wound was packed. No irrigations were given. In five cases convalescence was markedly prolonged because complicating factors developed; the average duration for the other 113 cases was forty-five days from the time the drainage was instituted to the time the wound was healed. Since the convalescent period after open drainage remains long, it seemed that hastening the obliteration of the cavity would be the only available means for shortening convalescence. The measures employed consisted of deep breathing exercises, blowing colored liquids from one Woulfe bottle into another, blowing up balloons or other variations of the same idea, all tending to produce forced respiratory movement. There is a rhythmic fall and rise of pressure in the empyemic cavity coincident with inspiration and expiration, and the lung can be felt to expand with each inspiration. Obliteration of the cavity in a unilateral process might be accelerated by producing the condition of compression of the other lung by artificial pneumothorax. This procedure has been employed in an additional twenty-one cases. From seven to ten days after the termination of the active pneumonic process, closed intercostal drainage is instituted, until which time no diagnostic punctures are made. The wall of the chest is prepared with iodine and alcohol at the dependent portion of the cavity (usually in the posterior axillary line). After infiltration of the wall of the chest with 1 per cent procaine hydrochloride, a small incision is made with a scalpel, and a trocar and cannula (No. 26 French) is plunged into the cavity. The trocar is removed, and a catheter, previously prepared and clamped at one end, is pushed through the cannula into the cavity. The cannula is then removed and a rubber diaphragm cap is passed over the tube down to the wall of the chest. This cap is sealed to the wall of the chest with collodion or rubber cement and reinforced with adhesive strapping. The catheter is also strapped securely to the wall of the chest and subaqueous drainage is provided for with a T tube, one end of which is connected to a reservoir containing 1 per cent diluted solution of sodium hypochlorite. Beginning on the second or third day, the empyemic cavity is irrigated with the solution every three hours night and day. From two to three days after drainage is begun, artificial pneumothorax is instituted on the unaffected side of the chest. After proper preparation, the skin and subcutaneous tissues in the sixth interspace in the midaxillary line are infiltrated with procaine and the pneumothorax needle is introduced into the pleural cavity. Air is then injected, 50 cc. at a time, and the intrapleural pressure is noted. Never more than 250 cc. is given to children at the first injection, nor is the positive pressure allowed to exceed 3 cm. of water at any time. The needle is then quickly withdrawn, the index finger is applied over the puncture wound and it is sealed with cotton and collodion. In forty-eight hours another 250 to 400 cc. is administered. Pneumothorax is maintained by successive injections with roentgenographic and fluoroscopic control as the guide until drainage has ceased, the lung is expanded and the empyemic cavity is obliterated. In the adults the average duration of drainage was 21.2 days and the average duration from the institution of drainage to healing was 25.5 days. The average duration of healing for the twenty-one cases of adults and children was 20.6 days. This method is not completely devoid of danger.

Plasma Exudation.—In the belief that it would be well to assemble data on the loss of plasma in burns, freezing, bile peritonitis, tissue autolysis in vivo, acute pancreatitis, pneumonia and pulmonary edema, intestinal manipulation, portal and mesenteric obstruction, externally strangulated colostomy loops and release of a constrictor of an extremity under one head, Harkins and Harmon have done so. They make no attempt to prove in each instance that the loss of plasma is the sole or even the chief factor in the resultant death. Toxic products or nervous reactions are always to be considered. Two factors make the exudation of a certain amount of fluid in these conditions of much more serious import than the loss of a similar amount of usually more watery fluid in certain so-called internal medical conditions. The first of these is the rapidity of the loss. In all these surgical conditions the loss of plasma-like fluid is of rapid occurrence, taking place in only a few hours. The transudates in ascites, pleural effusion, edema of the extremities, and the like, are usually of a more chronic type and are slower of formation. The second factor is the protein content, which is similar to blood plasma in these conditions but is low in the transudates occurring in ascites, pleural effusion and edema of the extremities. To epitomize, one can easily lose 2 liters of urine in a day but would not advisedly part with 2 liters of blood in the same time. There are traumatic conditions of a nature in which the blood vessels are injured to an extent that only, or chiefly, plasma rather than whole blood leaks out. Mechanical injuries in which vessels are cut or ruptured usually lead to loss of whole blood. The ten conditions discussed in which loss of plasma occurs represent a somewhat different type of trauma in which the injury involves especially the capillaries. Burns and freezing represent thermal trauma, while bile peritonitis, tissue autolysis in vivo and acute pancreatitis

may represent chemical trauma. In pneumonia and pulmonary edema the capillary injury may be either chemical or toxic. Intestinal manipulation is a form of mechanical trauma but depends on a continued mild trauma over a prolonged period rather than a sudden rapid gross trauma. In portal and mesenteric obstruction, externally strangulated colostomy loops and release of a constrictor of an extremity the chief factor seems to be capillary damage due to inadequate circulation. It thus seems that trauma of a thermal or chemical nature, mild continued mechanical type or due to inadequate circulation is the sort of trauma especially likely to lead to exudation of plasma-like fluid from the blood stream. In a variety of conditions there is a loss of plasma-like fluid from the blood stream in amounts approaching fatal losses of plasma in plasmapheresis experiments. The fact that usually the loss of plasma in the shocklike conditions is a little less in all instances than in shock due to plasmapheresis is suggestive of additional factors. In these various conditions the relative importance of loss of plasma as a lethal factor varies considerably. Loss of plasma-like fluid seems to be much greater in fatal experimental bile peritonitis than in the closely related peritonitis due to intraperitoneal implantation of autoclaved liver.

Georgia Medical Association Journal, Atlanta

26: 527-568 (Nov.) 1937

*The Tuberculosis Situation in the State with Reference to the State Sanatorium. D. T. Rankin, Alto.—p. 527.
Diagnosis of Pulmonary Tuberculosis. F. C. Whelchel, Alto.—p. 529.
Some Medical Aspects of Pulmonary Tuberculosis. H. E. Crow, Alto.—p. 531.
Indications for Surgical Treatment of Pulmonary Tuberculosis. D. C. Elkin and C. W. Strickler Jr., Atlanta.—p. 534.
Surgical Treatment of Tuberculosis. C. D. Whelchel, Gainesville.—p. 541.
Comparative Study of Pneumothorax Treatments in White and Negro Races. A. W. Hobby, Atlanta.—p. 542.
Medicine in Maelstrom. R. H. Chaney, Augusta.—p. 551.
Wake Up and Give. M. M. McCord, Rome.—p. 552.

Tuberculosis and the State Sanatorium.—Rankin believes that for every patient treated in the sanatorium ten are walking the streets and spreading the infection. The state department of health with its traveling clinic is endeavoring to find all the tuberculous cases in the state and especially the early ones. It is trying to educate the people, to make them tuberculosis conscious. Some of the counties have established sanatoriums and others have built portable shacks so that the patients may at least be isolated. The state tuberculosis society is running a sanatorium, is conducting a program of education and is helping furnish money for treatment to needy patients. The state sanatorium is rendering patients sputum negative and is training them how to live so as not to menace those with whom they come in contact. But too many unnecessary cases are developing. In other words, most of the results show not in prevention but in improvement and arrests of active cases. There is no way to force a person suspected of having tuberculosis to be examined or one known to have the disease to be treated. Vaccination is required against smallpox, diphtheria and typhoid, quarantine for cases of smallpox, diphtheria and other contagious diseases and isolation for leprosy, but for the disease that is far more contagious than leprosy, that kills nearly as many as typhoid, that takes years, not weeks, to recover from and even if arrested almost inevitably leaves the patient crippled so far as leading a normal, active, energetic life is concerned it is left strictly up to the pleasure and intelligence, or lack of it, of the patient himself as to what precautions, if any, he will take for the protection of his fellow man, or whether he will take treatment or not; few appear to care, and little if anything is done about it. Before much headway can be made to cut down the morbidity of tuberculosis, some plan must be worked out whereby persons with the open, active type can be isolated for as long a time as they are liable to spread the disease.

Indiana State Medical Assn. Journal, Indianapolis

30: 559-616 (Nov.) 1937

Anesthetic Agents and Methods Useful in General Practice. J. S. Lundy, Rochester, Minn.—p. 562.
Roentgenology as an Aid to Diagnosis of Lesions in the Upper Right Abdomen. B. H. Nichols, Cleveland.—p. 565.
Inflammatory Diseases of the Small Intestines (So-Called Regional Ileitis). B. D. Rosenak, Indianapolis.—p. 568.
Reminiscence. P. H. Weeks, Michigan City.—p. 573.
Efficiency of the Eyes. C. J. Rudolph, South Bend.—p. 574.

Iowa State Medical Society Journal, Des Moines

27: 561-608 (Nov.) 1937

Avoidance of Permanent Colonic Stoma in Surgery of the Colon. C. F. Dixon, Rochester, Minn.—p. 561.
What We Should Expect from Transurethral Prostatic Resection. W. K. Hicks, Sioux City.—p. 563.
Treatment of Trachoma. J. H. Allen, Iowa City.—p. 568.
Barbiturate Therapy and Cataract Surgery in Parkinsonism. M. J. Blaess, Marshalltown.—p. 571.
Relation of Gallbladder Disease to Certain Heart Conditions. J. W. Thornton, Lansing.—p. 573.
Preoperative and Postoperative Care. J. E. Brinkman, Waterloo.—p. 577.

Journal of Biological Chemistry, Baltimore

121: 373-820 (Nov.) 1937. Partial Index

Relation of Cystine and Methionine to Growth. Madelyn Womack, K. S. Kemmerer and W. C. Rose, Urbana, Ill.—p. 403.
*Cause of Sore Mouth in Nephritis. S. Bliss, New Orleans.—p. 425.
Production of Bacterial Enzymes Capable of Decomposing Creatinine. R. Dubos and B. F. Miller, New York.—p. 429.
Studies on Presence of Creatinine in Human Blood. B. F. Miller and R. Dubos, New York.—p. 447.
Determination by a Specific, Enzymatic Method of Creatinine Content of Blood and Urine from Normal and Nephritic Individuals. B. F. Miller and R. Dubos, New York.—p. 457.
Effect of Supplementary Methionine and Cystine on Production of Fatty Livers by Diet. Helen F. Tucker and H. C. Eckstein.—p. 479.
Effects of Anterior Pituitary Growth Preparation on Protein Metabolism. O. H. Gaebler and W. H. Price, Detroit.—p. 497.
Rate of Change of Alkali Reserve After Ingestion of Salts of Organic Compounds: II. Rate of Change of Alkali Reserve After Ingestion of Sodium Citrate and Sodium Bicarbonate. Jane Cape and E. L. Sevringhaus, Madison, Wis.—p. 549.
Chemistry of Lipids of Tubercle Bacilli: LI. Concerning Firmly Bound Lipids of Human Tubercle Bacillus. R. J. Anderson, R. E. Reeves and F. H. Stodola, New Haven, Conn.—p. 649.
Id.: LII. Composition of Acetone Soluble Fat of Bacillus Leprae. R. J. Anderson, R. E. Reeves and J. A. Crowder, New Haven, Conn.—p. 669.
Studies on Serum Phosphatase Activity: Parts I to V. S. J. Thannhauser, M. Reichel, J. F. Grattan and S. J. Maddock, Boston.—p. 697.
The Milk Clotting Action of Papain. A. K. Balls and S. R. Hoover, Washington, D. C.—p. 737.

Cause of Sore Mouth in Nephritis.—It seems that the severe ulceration of cheeks and tongue seen frequently in nephritic patients and nephrectomized dogs may be due to local irritation by ammonia. Bliss has found that tartar from the teeth of dogs contains urease. It is his opinion that ammonia is formed by the action of urease on the urea in saliva. Dogs with normal blood nonprotein nitrogen values do not have ulceration of the tongue and cheeks even though the teeth are coated with tartar. The ulceration of cheeks and tongue in his nephrectomized dogs is in just those locations at which the tissues lie against the teeth. Ulcerations clear up when tartar is removed from the teeth even though the blood nonprotein nitrogen remains elevated. Tartar scraped from the teeth of normal and nephritic dogs hydrolyzes urea solutions to ammonia in a few minutes, just as urease does. It was demonstrated that ammonia does actually damage such tissues.

Journal of Immunology, Baltimore

33: 337-418 (Nov.) 1937

Nonspecificity of Flocculative Phase of Serologic Aggregation. S. B. Hooker and W. C. Boyd, Boston.—p. 337.
Immunogenetic Studies of Species and of Species-Hybrids in Doves: Separation of Species-Specific Substances in Second Backcross. M. R. Irwin and L. J. Cole, Milwaukee.—p. 355.
Comparative Titrations of Antimeningococcus Serums Produced with Living Cells and with Broth Filtrates. Mary B. Kirkbride and Sophia M. Cohen, Albany, N. Y.—p. 375.
Fractions of the Human Group-Specific *A* Antigen. K. M. Wheeler and C. A. Stuart, Providence, R. I.—p. 393.
*Effect of Sulfanilamide (Para-Aminobenzenesulfonamide) on Group C Hemolytic Streptococcic Infections. C. V. Seastone, Princeton, N. J.—p. 403.
Anaphylaxis with Tobacco Mosaic Virus Protein and Hemocyanin. C. V. Seastone, H. S. Loring and K. S. Chester, Princeton, N. J.—p. 407.

Sulfanilamide and Streptococcic Infections.—Seastone discusses the effect of sulfanilamide on guinea pigs infected with hemolytic streptococci belonging to Lancefield's group C. Two strains were used, both of which were isolated from a naturally occurring disease in guinea pigs. Strain A was isolated from the chronic lymphadenitis known as "lumps," and strain B was isolated from a colony of guinea pigs infected with the chronic disease. Sixteen guinea pigs were each given about 5,000,000 organisms of the chronic strain A intradermally on

the left flank. They were divided into four groups. The first received no treatment, the second was treated immediately, the third and fourth were treated one and two weeks respectively after the inoculation. Treatment consisted in the oral administration of 50 mg. of sulfanilamide twice daily. It was discontinued on the thirtieth day of the disease. The animals receiving immediate treatment failed to develop any signs of disease during a period of forty days thereafter. However, about fifty days after the inoculation, two of the four began to show enlargement of the inguinal lymph nodes on the left, and sixty days after the inoculation these were well developed. The animals were killed and hemolytic streptococci were isolated from these abscesses. The course of the disease in the guinea pigs treated one and two weeks after inoculation was indistinguishable from that of the controls which had received no treatment. The intradermal injection of only a few (from ten to 100) organisms of the virulent strain B caused a local abscess in two or three days with surrounding redness and edema. The regional lymph glands were slightly enlarged and soft and the temperature was elevated. The abscess and enlargement of the lymph nodes progressed and the animal died in from five to ten days. The heart's blood culture was almost invariably positive. Control animals, which showed the characteristic elevation in temperature, died in from six to twelve days. The treated animals developed no significant febrile reactions, although for a few days after inoculation a slight induration and redness was present at the site of injection. This rapidly regressed. No enlargement of the lymph nodes occurred. Twenty-two days after the first inoculation the same dose of organisms was given, treatment being withheld. All the animals succumbed. Another group of four guinea pigs was inoculated three times with this lethal dose of organisms, the infection being prevented each time by means of sulfanilamide. Then each of the four guinea pigs received about 300 streptococci intradermally, treatment being withheld. The three animals which had shown no sign of chronic disease died in from five to seven days with hemolytic streptococci in the heart's blood. The remaining chronically infected guinea pig survived.

Journal of Urology, Baltimore

38: 421-508 (Nov.) 1937

Some Observations on Renal Capsule. H. C. Rolnick, Chicago.—p. 421.
Bilateral Renal Ectopia. E. K. Morgan and C. M. Stone, Brooklyn.—p. 427.
Bilharziasis of Ureter and Its Pathognomonic Roentgenographic Appearance. V. Vermooten, Johannesburg, South Africa.—p. 430.
Ureteral Anomalies, with Especial Reference to Partial Duplications with One Branch Ending Blindly: Report of Two Cases with Renal Obstruction Cured by Surgical Resection. A. Harris, Brooklyn.—p. 442.
Scrotal Hernia of Ureter, Associated with Unilateral Fused Kidney: Case Report. R. L. Dourmashkin, New York.—p. 455.
*Successful Radical Perineal Resection of Bladder Neck for Carcinoma. C. L. Deming, New Haven, Conn.—p. 468.
Traumatic Injuries of Bladder: Report of Twenty-Seven Patients Operated on. A. R. Stevens and W. R. Delzell, New York.—p. 475.
*Tertiary Prostatic Hypertrophy: Unusual Case Report. C. A. W. Uhle, Philadelphia, and P. D. Melvin, Miami, Fla.—p. 487.
Leukemic Infiltration of the Prostate. M. Jacobi, C. E. Panoff and J. Herzlich, Brooklyn.—p. 494.
Fibrolipoma of the Penis: Case Report and Review of Literature. J. T. Gernon and C. M. McKenna, Chicago.—p. 500.
A Urethral Meatoscope. R. J. Hubbell, Kalamazoo, Mich.—p. 503.
Ribdam: New Packing for Use After Enucleation of the Prostate. J. A. Hyams, New York.—p. 504.

Resection of Neck of Bladder for Carcinoma.—Deming believes that radical perineal resection for carcinoma of the neck of the bladder should be added to the surgeon's armamentarium. This method of surgical treatment may be used in a limited number of cases and has certain advantages over other forms of treatment. Immediate relief is given to the patient. He does not have a long period of spasm of the trigon or neck of the bladder. Dysuria is a negligible factor. The preservation of the external sphincter gives complete control of urination, with a normal maintenance of the capacity of the bladder. A patient with cancer of the neck of the bladder treated with radical perineal excision of the neck of the bladder, part of the trigon, prostate and seminal vesicles is reported well after a six year period. Restoration of normal urination was secured. The comfort of the patient after this operation was extraordinary as compared with the long period of dysuria usually seen after radium treatment.

Tertiary Prostatic Hypertrophy.—It is the impression of many that recurrence of benign prostatic hypertrophy, following a previous suprapubic or perineal operation, is unique. That this assumption is fallacious is evidenced by the statements of men who have had wide clinical experience in prostatic work. However, two recurrences are uncommon and for its unusual interest Uhle and Melvin cite the history of their patient who was subjected to four operative procedures (during a period of nine years and four months) for the relief of prostatic obstruction. The frequency of recurrence, according to several investigators, varies between 1 and 2 per cent. The surgical pathology of benign prostatic enlargement precludes the fact that the prostate is removed at operation. Adenomatous tissue is enucleated. The adenomas, during their period of growth, expand and compress prostatic tissue into a thin shell resembling a capsule. With pressure removed, the prostatic tissue either remains atrophic or regenerates to resume its normal size once again. Therefore it seems logical to assume that the same etiologic factor or factors causing the original growth may also explain the recurrence of prostatic hypertrophy. Another factor in recurrence, and one receiving theoretical consideration from various authors, is the failure to notice or the incomplete removal of small spheroids of adenomatous tissue at the first operation. If the blood supply is not injured, these small spheroids are capable of regeneration to the degree of interfering with the dynamics of micturition.

Medical Annals of District of Columbia, Washington

6: 305-336 (Nov.) 1937

Present Status of Tuberculosis in the District of Columbia. G. C. Ruhland and C. C. Dauer, Washington.—p. 305.
Medical Uses of Ergotamine Tartrate. H. H. Hussey, Washington.—p. 309.
Value of Combining Sedation of the Central and Autonomic Nervous Systems in Treatment of Epilepsy. J. W. Watts, Washington, and G. A. Schwarz, New York.—p. 315.
Methods of Diagnosis of Female Endocrinopathies. J. Kotz and Elizabeth Parker, Washington.—p. 321.
New Type of Trephine Burr for Simplifying Neurosurgical Technic. J. J. Shugrue, Washington.—p. 328.

Pennsylvania Medical Journal, Harrisburg

41: 79-176 (Nov.) 1937

*Peptic Ulcer. F. H. Lahey, Boston.—p. 79.
Acute Osteomyelitis in Children. R. L. Ellis, York.—p. 86.
Meddlesome Obstetrics. R. G. Emery, Washington.—p. 88.
The General Practitioner and the Neurotic Child. R. H. Israel, Warren.—p. 91.
The Fad of Alkalization and Its Relation to Renal Lithiasis. W. J. Ezickson, Philadelphia.—p. 94.
Malignancy of the Lung. H. W. Bernhardy, Rochester.—p. 96.

Peptic Ulcer.—On the basis of an analysis of 3,000 cases of peptic ulcer treated at the Lahey Clinic, Lahey concludes that all peptic ulcers, except those which are true surgical emergencies, are best submitted to the gastro-enterologist for investigation and a primary trial of management. The surgical indications are largely those related to failure under medical management, such as persistence of pain, perforation, pyloric obstruction, hemorrhage and a suggestion of a malignant condition in an ulcerating lesion. Gastro-enterostomy is no longer justifiable as a routine method of treating peptic ulcer surgically. Subtotal gastrectomy is the operation that is followed by the highest percentage of patients having low gastric acid values, by the lowest incidence of gastrojejunal ulcer and with the fewest digestive difficulties. Subtotal gastrectomy is not to be applied unreservedly to all patients with ulcer.

Southwestern Medicine, Phoenix, Ariz.

21: 377-424 (Nov.) 1937

The British Social Security Act, with Especial Reference to the Panel System. R. J. Stroud, Tempe, Ariz.—p. 377.
Importance of Early Recognition of Biliary Tract Affections. E. A. Campbell, Albuquerque, N. M.—p. 379.
Congenital and Acquired Vesical Neck Obstruction in Male Children. H. T. Low, Pueblo, Colo.—p. 381.
Eye Injuries from Foreign Bodies. W. J. Smith, Phoenix, Ariz.—p. 384.
Torsion of the Testicle. K. D. Lynch and R. F. Thompson, El Paso, Texas.—p. 388.
Gastro-Intestinal Dysfunction. B. A. Rhinehart, Little Rock, Ark.—p. 391.
Syphilis, Ulcer and Carcinoma of the Stomach: Case. F. J. Milloy, Phoenix, Ariz.—p. 398.
Medical Annals of Arizona: Carlos Montezuma, M.D. O. H. Brown, Phoenix, Ariz.—p. 400.
The "Last Days" of Carlos Montezuma, M.D. R. J. Stroud, Tempe, Ariz.—p. 404.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

49: 465-526 (Nov.) 1937

Studies of Photosensitization by Porphyrins. H. F. Blum and N. Pace.—p. 465.
Lipstick Dermatitis: Report of Case Due to Eosin. F. F. Hellier.—p. 485.
*Occurrence in Humans of Contagious Pustular Dermatitis of Sheep ("Orf"). G. A. G. Peterkin.—p. 492.

Contagious Pustular Dermatitis.—Peterkin reports five cases of contagious pustular dermatitis of sheep ("orf") in human beings. The only difference that he observed between the lesions produced in animals experimentally and those found in human beings is that there seems to be in the human being a tendency for the lesions to be umbilicated. The progress of the disease seems to run the following course: The first lesion to appear is a dark red papule, which grows to any size from threepence to half a crown. This is quite hard and as a rule painless. Gradually the papule begins to resemble a huge red molluscum contagiosum tumor, with a marked umbilication. This depressed center is covered with thin white skin and contains clear exudate. This exudate gradually becomes purulent, probably owing to secondary infection, and granulations soon heap up. This stage is often painful. If the tumor is dressed with antiseptics, it tends to shrivel up in a few weeks, without any purulent discharge or granulations appearing.

British Journal of Radiology, London

10: 765-828 (Nov.) 1937

*Place of X-Rays in Treatment of Certain Forms of Chronic Arthritis. F. Hernaman-Johnson.—p. 765.
Radiating Surfaces. J. van Roojen.—p. 781.
Brachymesophalangy and Syndactyly in a Telegu. J. H. Barrett.—p. 817.

X-Rays in Treatment of Chronic Arthritis.—Hernaman-Johnson discusses those forms of arthritis in which x-rays should be given a trial. Hypertrophic noninfective osteo-arthritis (monarticular) is amenable to roentgen therapy, provided no predisposing factors are left out of account. Patients should never be rejected because roentgenograms reveal an advanced state of disease. Functional disability alone should not cause one to take a hopeless view. Actual ankylosis will defeat any efforts to restore function except by surgical means, but ankylosis is comparatively rare and it is doubtful whether it can occur in true hypertrophic arthritis. Failure to benefit by roentgen treatment in hypertrophic noninfective arthritis may occur for no discoverable reason, but some common causes of failure are an increasing obesity, static deformity, lack of active exercises and passive movements and focal infection. Infective arthritis (monarticular), when first seen in its chronic stage, is to be differentiated from the noninfective form rather by the history than by the x-ray appearances. The x-ray picture may be indistinguishable from that of hypertrophic arthritis, or it may show greater loss of cartilage, rougher joint margins and less osteophytic formation than is usual in the noninfective form. The treatment of these cases is more difficult than is that of the noninfective monarticular arthritis. If x-rays are used, the dosage must be very carefully graded according to the amount of active inflammation present. In the chronic stages, dosage may be used as in the hypertrophic form. Temporary improvement is perhaps the rule, but genuine arrest is hard to attain. Many of these joints ultimately have to be excised, with a view either to the making of a false joint or to the production of a bony ankylosis. There is little doubt that the lumping together of such cases with those of the noninfective form, merely because the late x-ray appearances are similar, has been detrimental to a proper appreciation of the beneficial effects of roentgen treatment. An analysis of the author's series of eighty cases of noninfective arthritis treated showed 25 per cent functionally cured, 40 per cent greatly improved and the remainder only slightly, or not at all, benefited. In hypertrophic noninfective osteo-arthritis, 150 roentgens is given to the affected joint twice a week for three weeks (first series). If some lessening of pain results, the same treatment is continued for a further three weeks. If no relief occurs the dosage in the second series of six treatments may be increased to 300 roentgens per sitting; 180 kilovolts, 0.5 of copper filter, 40 cm. focus skin distance and a field of from 25 to 30 cm. in diameter; anteroposterior, postero-anterior and lateral areas are used. Such treatment seldom produces any constitutional disturbance unless arthritis of the spine is concerned. In the latter case the field should be reduced to from 10 to 12 cm. in the long axis of the body if the patient complains of general discomfort. As to further treatment, at least two more full courses of twelve sittings should be given at intervals of three months, no matter how well the patient feels, and thereafter less frequently for from two to three years. If improvement at the end of six weeks is small or absent, it is desirable to persist. X-rays applied locally to individual joints in rheumatoid arthritis (polyarthritis) may give some temporary relief, but the progress of the disease is not checked. The malady is essentially constitutional, and, if it is ever to be dealt with successfully, it must be by some form of constitutional treatment.

Glasgow Medical Journal

10: 193-244 (Nov.) 1937

The Chemistry of Bacterial Action in Relation to Enzyme Activity and Human Pathogenicity. J. W. Chambers and R. D. Stuart.—p. 193.
The Mechanism of Headache. J. E. Paterson.—p. 210.

Journal of Mental Science, London

83: 489-608 (Sept.) 1937

Some Observations on the Care of the Insane. D. McRae.—p. 489.
Some Remarks on Physiology of Cerebral Circulation. F. L. Golla.—p. 505.
Cerebral Ischemia and Mental Disorder. F. A. Pickworth.—p. 512.
Circulatory Factor in Pathogenesis of Mental Disorder. E. Krapf.—p. 534.
Psychologic Implications of Functional Circulatory Disorder. E. Guttmann.—p. 542.
Psychoses Associated with Hypertension, Arteriosclerosis and Heart Failure. W. Mayer-Gross.—p. 551.

Lancet, London

2: 1061-1118 (Nov. 6) 1937

Orthopedic Surgery: Retrospect and Forecast. W. R. Bristow.—p. 1061.
*Chemotherapy of Streptococcic Infections: Particularly Streptococcic Tonsillitis. A. Smith.—p. 1064.
*Heart Block in Coronary Thrombosis. J. D. O. Kerr.—p. 1066.
Pentothal Sodium in Intravenous Anesthesia. F. B. Mallinson.—p. 1070.

Chemotherapy of Streptococcic Infections.—Smith has used sulfanilamide and similar preparations in the treatment of two cases of hemolytic streptococcic arthritis of the hip joint, thirty-nine cases of streptococcic tonsillitis among inpatients and the staff, and six cases of streptococcic cervical adenitis and cellulitis in outpatients who had had tonsillitis. The *p*-aminophenylsulfonamide and *p*-benzylaminobenzenesulfonamide were equally valuable in the treatment of streptococcic tonsillitis, but the latter was somewhat less toxic. Larger doses than those usually advised were found advantageous. The combined administration of sulfanilamide and serum was found useful. The sulfonamides had no prophylactic value in checking the spread of tonsillitis under epidemic conditions. Infection by the hemolytic streptococcus was more amenable to treatment by the sulfonamides than infection by Streptococcus viridans.

Heart Block in Coronary Thrombosis.—Kerr presents a review of previous reports of heart block in coronary thrombosis. In the 1,436 reported cases of coronary thrombosis the average incidence of heart block proved to be 7.4 per cent. Among the case records of the cardiac department of the London Hospital and others from a consulting practice there were thirteen cases of coronary thrombosis complicated by heart block. In these thirteen patients heart block first appeared under observation during the clinical course of coronary thrombosis: Four had a slight degree of a prolonged PR interval, four had partial and five complete heart block. Seven made good clinical recoveries, with disappearance of the block. Of the partial heart block group, two died within a few weeks and one was untraced. The remaining three died, one in an Adams-Stokes attack a week after the onset, the other two six weeks and eighteen months respectively after the onset. Coronary thrombosis has to be included among the causes of chronic heart block seen either because of bradycardia or because of clinical symptoms with or without Adams-Stokes attacks. In

any collected series of cases of clinical heart block, those of acute onset from this cause should be considered separately. The conductive tissues may escape completely in an extensive cardiac infarction, while a localized occlusion of the vessels supplying the node and bundle may occur, creating too slight a disturbance to be recognized clinically as a cardiac infarction, though sufficient to produce heart block. Although the prognosis of coronary thrombosis in general is adversely affected by the complication of heart block, clinical recovery and disappearance of the block are by no means uncommon.

Chinese Medical Journal, Peiping

52: 479-622 (Oct.) 1937

*The Heart in Severe Anemia. C. L. Tung, W. N. Bien and Y. C. Ch'u, with collaboration of S. H. Wang and W. S. Ma.—p. 479.
Obstetric Criteria in North China: II. Weights and Measurements of the Mature New-Born Child. G. King and T'ang Yü Teh.—p. 501.
Physical Traits of Peiping Children: I. Stature and Weight Measurement from One Month to Three Years of Age. R. A. Guy, C. C. Chiang, H. H. Huang and K. S. Yeh.—p. 507.
Fractures of the Skull. Y. C. Chao and S. T. Kwan.—p. 519.
Studies in Liver Function of the Chinese. W. W. Cadbury and T. Y. Ting.—p. 531.
*Insulin Shock Treatment of Schizophrenia: Preliminary Report. F. G. Halpern.—p. 541.

The Heart in Severe Anemia.—The interest of Tung and his associates on the effect of prolonged, severe anemia on the cardiovascular system was aroused in 1933, when one of them observed marked cardiac enlargement and congestive failure in a patient with Banti's disease and severe hypochromic anemia. They observed ten patients suffering from severe anemia (hemoglobin about 2.5 Gm., or 17 per cent), without any other discoverable factor that might cause heart disease, for the effects of such anemia on the cardiovascular system, with clinical, x-ray and electrocardiographic studies. In addition, venous pressure by the direct method and the arm to tongue circulation time were determined in most of the cases. Three patients showed marked cardiac enlargement with little or no evidence of congestive failure. Six showed marked cardiac enlargement and marked congestive failure. One had a normal heart. Cardiac enlargement rapidly disappeared with rest and an increase of the hemoglobin toward normal, and the heart assumed normal size and shape when the blood became normal. Diastolic cardiac murmurs encountered in two patients during the height of anemia disappeared when the anemia disappeared. All patients except one had sinus tachycardia and large pulse pressure. Six patients presented physical evidence of marked congestive heart failure, including the elevation of venous pressure. The relative duration of electrical systole was prolonged. In spite of elevated venous pressure the circulation time remained normal. It is concluded that marked cardiac enlargement and marked congestive heart failure may result from prolonged, severe anemia alone, particularly in individuals who have extra demands on their circulatory system (physical exertion, fever, pregnancy, parturition). Both cardiac enlargement and cardiac failure in such cases disappear rapidly when the anemia is cured. "Anemic heart" should be considered a clinical entity.

Insulin Shock Treatment of Schizophrenia.—Of the schizophrenic patients treated by Halpern by the insulin shock method, only eight have completed the treatment, while others are still under treatment. The patients were unselected and were taken into treatment without regard to the duration and the type of schizophrenia. Although five of the eight cases were chronic, the results are very encouraging. There has been no fatality, although severe collapse and epileptic fits have been encountered which, fortunately, could be stopped in time. Half of the patients have had complete remission, one good remission, one remission with a defect (that is, with social fitness but remaining schizophrenic changes) and two partial improvement but without social fitness. The paranoid form of schizophrenia gave the best response to treatment. Likewise two cases of acute schizophrenia reacted well. Less favorable than the reaction of paranoid and acute schizophrenias to the treatment were the two patients with catatonia, in one of whom a good remission and in the other a remission with residual defect was obtained. Although the duration of the disease was not longer than in the two cases of the paranoid type, the treatment took a much longer time than in paranoid schizophrenia to effect remission.

Journal de Chirurgie, Paris

50: 737-892 (Dec.) 1937

*Is Infiltration of Stellate Ganglion Justified in Pulmonary Embolism? R. Leriche, R. Fontaine and L. Friedmann.—p. 737.
*Traumatic Serous Meningitis and Encephalic Arachnoiditis. P. Puech and E. Krebs.—p. 749.
Renal Lithiasis of Hypercalciuria. M. Roux.—p. 781.

Infiltration of Stellate Ganglion in Pulmonary Embolism.—Leriche and his associates reach the conclusion that infiltration of the stellate ganglion should be resorted to as quickly as possible in all pulmonary embolisms. The choice of the side is determined by the pain, provided it is distinct, but, if there is no indication of the localization of the embolism, the infiltration should be bilateral. The infiltration of the stellate ganglion is justified by the important part played by the vasomotor reflexes in the mechanism of death. Anatomopathologic studies in 225 cases of fatal pulmonary embolisms revealed that in the majority death is due to massive embolism of the pulmonary artery, either of the trunk itself or of the right and left branches. In these cases, that is, in about two out of three cases, the functional therapy is ineffective. If an embolism appears under conditions in which an embolectomy can be made at once, this intervention can always be tried. However, this requires a fortunate combination of circumstances which are not often found together. In pulmonary embolisms in which the services of surgical specialists are not available, the infiltration of the stellate ganglion is indicated. Always practicable, it is the method capable of counteracting the associated vasomotor disorders which aggravate the mechanical difficulties of the pulmonary circulation. It represents a notable therapeutic progress. Even the embolisms that occur under conditions in which a Trendelenburg operation is considered can probably be benefited by infiltration of the stellate ganglion, performed by the intern on duty, at the appearance of the first alarming signs, while awaiting the arrival of the surgeon. The authors conclude that physicians should master the technic of this method as they do that of the intracardiac injections. All that is required is a syringe of 10 cc. capacity, an ampule with a 1 per cent solution of procaine hydrochloride without epinephrine and a needle 10 cm. in length.

Traumatic Serous Meningitis and Encephalic Arachnoiditis.—Puech and Krebs report that in a series of forty-six cases of cerebral traumatisms, which were surgically treated by them, they observed twenty with serous meningitis or traumatic arachnoiditis. In spite of the alarming condition of the injured, they did not have a case of surgical fatality and the patients benefited by the intervention. The authors classify the twenty cases in two groups. In the first group the meningitis develops almost immediately, whereas in the second group it develops later. Each of these groups is again divided into subgroups. Taking up the first main group, the authors give their attention first to the diffuse and then to the localized cases of serous inflammation of the arachnoid and pia mater and then to the cases of internal hydrocephalus. They show that the nature of the intervention is determined chiefly by the trephine puncture. In some of the localized cases of early meningitis a simple trepanation may suffice. In describing some of the case histories, the authors also show illustrations of their surgical interventions. Following a discussion of the different groups of cases, the authors present a general discussion of the diagnosis, the pathologic anatomy and the pathogenesis. Concluding, they once more stress the favorable results that they obtained with their surgical interventions; they operated on some patients who were in complete coma and in whom death seemed only a question of hours. All the patients again became normal or almost normal.

Presse Médicale, Paris

45: 1707-1730 (Dec. 1) 1937. Partial Index

Is the Phenomenon of Arthus an Anaphylactic Phenomenon? A. Besredka.—p. 1712.
*New Reaction for Study of Lipoids: Lipoidemia. E. Chabrol and R. Charonnat.—p. 1713.

New Reaction for Study of Lipoids.—Chabrol and Charonnat state that their studies on the phosphovanillin reaction have led them to search for the variants that can be introduced by heating and the addition of sulfuric acid. To bring into evidence cholalic acid they, together with Cottet, aimed

at isolating the effects of cholesterol and of fatty acids. It is easy to disclose the latter substances by preceding the phosphovanillin reaction with the action of concentrated sulfuric acid at the temperature of the boiling water bath and, at the end of this treatment, it is the cholalic acid which disappears to cede the place to a color reaction, depending on cholesterol, nonsaturated fatty acids (oleic, linoleic), certain alcohols or higher aldehydes. If the cholalic acid ceases to interfere in the sulfophosphovanillin reaction, its congener, desoxycholic acid, plays only a small part beside the other substances. The authors adopted the following technic: One tenth cc. of the liquid that is to be tested is added to 4.9 cc. of concentrated sulfuric acid (specific gravity 1.84); then follows heating for ten minutes in the boiling water bath. After cooling, 0.4 cc. of the mixture is combined with 3.6 cc. of concentrated phosphoric acid (specific gravity 1.71); then 1 cc. of an aqueous solution of vanillin (0.6 in 100) is added. A rose tint develops gradually, which can be observed by the colorimetric procedure at the tenth minute, cobalt phosphate being taken as the scale of standards. The authors express the figures in cholesterol, after having fixed the equivalents which it is easy to establish between more or less diluted alcoholic solutions of this substance and the numbers of the color scale. The figures thus obtained correspond not only to the free and esterized cholesterol but also to the nonsaturated fatty acids (oleic and linoleic) which esterize cholesterol or which play a part in the fatty substances and in the lecithins. The authors reemphasize that cholalic acid does not produce the reaction but that desoxycholic acid can have a small part. They employed the test in 175 cases. Bile gave strong sulfophosphovanillin reactions. More than 20 Gm. of lipoids, expressed as cholesterol, can be detected. The corresponding figures determined by the reaction of Liebermann-Grigaut were between 0.5 and 1.25 Gm. per thousand. There exists no proportionality between the results of the latter reaction and the reactions obtained by the sulfophosphovanillin reaction. A tabular report indicates this clearly. The same discrepancies appear if the two tests are made on the blood serum. In view of the fact that considerable differences exist between the results obtained when the subject is fasting and when a fatty meal has been taken, the authors demand that the test be made in the morning, when the patient is still fasting. Extremely strong sulfophosphovanillin reactions of the blood serum were obtained in various clinical conditions. The maximum figure of 12 Gm. per thousand was noted in a milky serum, which revealed 2.5 Gm. of cholesterol by the technic of Grigaut, in which Harispe was able to detect a total lipoid content of 24 Gm. The patient in question was one with cholemia without icterus, in whom the liver was enlarged and sensitive. The authors also detected 11.5, 9, 8 and 6 Gm. per thousand in icteric patients who had diabetes, biliary cirrhosis and pancreatic cancer, respectively. The smallest figures, from 0.75 to 1.25 Gm. per thousand, were detected in the more or less cachectic patients with cirrhosis and in the patients who had been weakened by several days of repeated attacks of hepatic colic. In the majority of the examined cases (109 of 161) the figures were between 2 and 4 Gm. per thousand. The authors reach the conclusion that the sulfophosphovanillin reaction provides valuable information about the metabolism of the nonsaturated fats and about lipoidemia and cholesterolemia.

Jahrbuch für Kinderheilkunde, Basel

150: 193-256 (Nov.) 1937

Investigations on Vitamin C Metabolism in Lactating Women: Degree of Physiologic and Pathologic Saturation of Human Organism with Vitamin C. T. Baumann.—p. 193.
*Leukemia in Nurslings. O. Saxl.—p. 228.
*T Factor. E. Schiff and C. Hirschberger.—p. 247.

Leukemia in Nurslings.—Saxl reports five cases of leukemia in nurslings but says that leukemia is comparatively rare during infancy. One of the cases reported was so-called chloroma. The disorder began during the eighth month of life, the patient being one of the youngest known. He suggests that the term chloroma be abandoned and leukemic myelocytoma or leukemic lymphocytoma employed. Another one of the reported cases concerns a nursling in whom an acute leukemia was detected at the age of 4½ months. The mother of this nursling was syphilitic, but the child was free from manifest signs of syphilis. The child died with the symptoms of ileus caused by invagination of the leukemic infiltrates. Leukemia in a boy, aged 10, likewise terminated in death by ileus. The author further reports a case of myeloid leukemia in a nursling in whom symptoms of the disorder were already evident at the age of 6 weeks. It is probable that syphilis played a part in the pathogenesis of this case. Roentgen irradiation produced a temporary remission in this case. Another of the reported cases was one of myeloid leukemia in a nursling who was under observation from birth. At first this nursling presented signs of anemia and the subleukemic blood picture developed gradually. In antithesis to these cases the author presents a case of Jaksch-Hayem's pseudoleukemia which, after prolonged hospitalization, presented a leukemoid blood picture. This case demonstrates the difficulty of the differentiation between true leukemia and pseudoleukemia.

T Factor in Sesame Oil.—Schiff and Hirschberger investigated the increase in the number of thrombocytes under the influence of medication with the T factor. Vehicles of the T factor were either pure sesame oil or vitamin A in sesame oil. Investigations were made on twenty children and sixty-three rats. The observations indicated that sesame oil may be considered as having an adequate amount of the T factor if the daily administration of two drops to young rats (30 Gm.) or of twenty drops to healthy children produces, in three or four weeks, a doubling or a considerable augmentation of the number of platelets. The author says that as regards the thrombocytosis there is no difference between the two oils. The fact that the sesame oil containing the vitamin A (vogan oil) caused no greater increase in the number of thrombocytes and the fact that olive oil, which contains the same amount of vitamin A as does the vogan oil, exerted no influence whatever on the number of thrombocytes indicate that not the vitamin A causes the thrombocytosis but rather the T factor, which is found in sesame oil.

Giornale di Batteriologia e Immunologia, Turin

19: 433-576 (Oct.) 1937. Partial Index

Researches and Observations on Amount of Bacteria in Pasteurized and Unpasteurized Butter. P. E. Perini.—p. 433.
Researches on Pathogenicity of Bacillus Mesentericus Vulgatus. A. D'Agata.—p. 471.
Bactericidal and Bacteriostatic Properties of Phenylmercuric Nitrate. U. di Aichelburg.—p. 479.
Therapeutic Uses of Cod Liver Oil Ointment. E. Caserio.—p. 517.
Nakagawa Takasugi and Sato Test in Cancer. L. Montagnini.—p. 525.
*Influence of Short Waves on Pathogenic Bacteria. T. Ozzano and C. Re.—p. 535.

Influence of Short Wave Irradiation on Bacteria.—Ozzano and Re prepared two series of tubes which contained suspensions of several species of pathogenic bacteria. The tubes for the experiment were submitted to irradiations with waves 4.3 and 7.36 meters long, for thirty minutes. The controls were left in the incubator at a constant temperature of 98.6 F. Immediately after the irradiation, smear cultures were made with the experimental and control suspensions. After the preparation of smear cultures the experimental and control tubes were left in the incubator and the experiment was repeated one, four, six, twelve and fifteen hours after the first irradiation. The results as to the development and changes in the morphology and biologic properties of bacteria were observed in the smear culture suspensions twenty-four or thirty-six hours after they were prepared. In general, they were the same for the two bacterial suspensions. The irradiations sometimes stimulated and sometimes inhibited the development of bacteria. The effect was transient because of the extraordinary capacity of bacteria to regenerate. According to the authors, short wave irradiations have no selective specific action on bacteria. They act in an abiotic way by increasing the temperature of the environment of bacteria.

Pediatria, Naples

45: 1053-1106 (Dec. 1) 1937

Infant Mortality in Naples from 1931 to 1935. G. Buonomini.—p. 1053.
*Lymphocyte-Monocyte Index in Pulmonary Tuberculosis in Children. G. Murano.—p. 1066.
Favism in Rome: Five Cases Recently Observed with Especial Reference to Treatment. I. Biddau.—p. 1086.

Lymphocyte-Monocyte Ratio in Pulmonary Tuberculosis.—According to Murano, the lymphocyte-monocyte ratio in the blood of normal children diminishes as children grow up. It varies between 5.5 and 6.2 between the ages of 2 and 3 years,

between 3.6 and 5 between the ages of 4 and 9 years and between 3 and 5 in older children. The author made determinations of the variations of the ratio in the blood of forty-five children between the ages of 2 and 11 years who were suffering from pulmonary tuberculosis. The ratio varies in relation to the clinical form of pulmonary tuberculosis and the seriousness of the tuberculous lesion. It is increased in biliary and tracheobronchial adenopathies which are associated with toxemia and in epituberculous and perifocal regressive infiltrations. It is diminished in infiltrations of the lobar type (the so-called lobitis) and in ulcerocaseous and miliary forms of pulmonary tuberculosis. Whereas the increase of the ratio depends on the presence of lymphocytosis, which originates in defensive reactions of the body, its decrease depends on the presence of monocytosis and lymphopenia. The lymphocyte-monocyte ratio is of diagnostic value, in relation to the clinical form, evolution and intensity of pulmonary tuberculosis in children. However, it has no prognostic value.

Klinische Wochenschrift, Berlin

16: 1593-1632 (Nov. 13) 1937. Partial Index

Clinical Significance of B Avitaminoses. A. Meyer.—p. 1593.
Chemotherapy in Connection with Problem of Carcinoma. M. Oesterlin.—p. 1598.
Roentgenologic Aspects of Perforations of Digestive Tract. B. W. Ercklentz.—p. 1606.
Type Distribution of Extrapulmonary Pneumonococcic Diseases. B. Kemkes.—p. 1609.
Treatment of Bronchopneumonia Patients with Neoarsphenamine. B. Ebenius.—p 1611.
*Calcium Therapy of Lead Poisoning. H. Taeger.—p. 1613.
*Clinical Experiences with "Citrin" (Vitamin P). S. Lajos.—p. 1615.

Calcium Therapy in Lead Poisoning.—Taeger follows a review of the literature on calcium therapy of lead poisoning with a critical evaluation of this therapy. He shows that all interventions in the process of lead poisoning, be they measures to mobilize lead (potassium iodide, acidification or alkalization) or the administration of calcium, result in the mobilization of lead. For this reason, extreme caution is necessary in the therapy of lead poisoning. He too observed calcium deficiency in the erythrocytes of patients with lead poisoning and thinks that, in order to reestablish normal conditions, the administration of calcium is necessary but that it must be done with great caution. The most essential point in the treatment of lead poisoning is to prevent a further resorption of lead. In case of severe symptoms of intoxication (colics, paralysis and so on) all measures that mobilize lead are strictly contraindicated. After the first acute signs of intoxication have disappeared, calcium should be given in order to compensate for the calcium deficiency. However, the calcium should not be given in large doses. Milk, which contains calcium and phosphates in a suitable ratio, should be given in gradually increasing quantities. The daily quantity of milk should not exceed 1 liter. Later, a small amount of calcium gluconate may be given by mouth. Large doses, as well as the intravenous administration of calcium, are to be avoided.

Experience with Vitamin P.—Lajos points out that Szent-Györgyi and his collaborators isolated from lemons a crystalline substance which they designated as "citrin." Since these investigators demonstrated that the administration of citrin exerts a favorable effect on the resistance and permeability of the capillaries in cases of vascular purpura, they applied to "citrin" the term of permeability vitamin or vitamin P. This substance is a mixture of the glucosides that belong to the group of the flavones. The author reports his therapeutic experiences with vitamin P (citrin). He says that vitamin P is a strongly active pharmacologic substance of great therapeutic value. It increases the capillary resistance and decreases the permeability of the vessels. It is valuable in the treatment not only of vascular purpura but also of hemorrhagic nephritides of different origins. In the latter conditions it quickly arrests the hematuria and also improves the general condition. The author thinks that vitamin P might be of prophylactic value in disorders in which there is danger of nephritis. In other disorders that are accompanied by hemorrhages the administration of vitamin P does not effect such a noticeable improvement in the clinical picture, although there may be an increase in the capillary resistance and a reduction in the permeability of the vessels.

Zeitschrift für Krebsforschung, Berlin

46: 313-378 (Sept. 30) 1937

*Investigations on Cancer Metastases. H. E. Walther.—p. 313.
Carcinogenic Action of 1.2 Benzpyrene. J. Klinke.—p. 334.
Immunization Experiments with Brown-Pearce's Rabbit Tumor. W. Raab.—p. 343.
Growth and Differentiation of Carcinoma of Lactiferous Duct in Main Tumor and Metastasis. H. Dabelstein.—p. 355.
Acquired Resistance of Lung of Rat Against Metastases of Jensen Sarcoma. E. Schairer.—p. 364.

Cancer Metastases.—According to Walther, the hematogenic route is the deciding factor in the dissemination of cancer. In this respect there are only differences in degree between the connective tissue tumors and the epithelial tumors. Depending on the position in the circulatory system, the organs are classified into four groups, and accordingly there are four types of metastatization: (1) the pulmonary type, (2) the hepatic type, (3) the portal vein type and (4) the vena cava type. These four types are characterized not only by the type of hematogenic dissemination but also by the susceptibility to metastases. The capillary regions of the organism, depending on their position in the circulatory system, represent filters of the first, second or third class for the hematogenic dissemination. Whereas the topography of the dissemination is dependent on the aforementioned types of metastatization, the quantitative character of the metastatization (density of dissemination) is determined by the specific characters of the cancer cells and the structure of the tumor. The author thinks that there are no convincing proofs for the occurrence of a true retrograde dissemination. He thinks that a large number of the cases with alleged retrograde lymph node metastases are cases of continuous dissemination. On the basis of his experiences, he concludes that this generally unsatisfactory hypothesis can be abandoned. In the majority of cases he was able to demonstrate that diseased lymph nodes which are not in the region of the primary tumor were regional metastases of an organ that had become involved by the hematogenic route. Whereas a retrograde transport in the lymph vessels appears improbable for purely anatomic reasons, the possibility of a temporary reversion of the venous blood stream must be conceded; but even this theoretical possibility is of only slight practical significance.

Zentralblatt für Gynäkologie, Leipzig

61: 2369-2416 (Oct. 9) 1937

Unilateral Removal of Ovaries and Its Sequels. P. Caffier.—p. 2370.
*After-Treatment of Menopausal Hemorrhages with Roentgen and Radium Rays. W. von Massenbach.—p. 2377.
Significance of Decidual Transformation of Uterine Mucosa for Diagnosis of Extra-Uterine Pregnancy. H. Schneider.—p. 2381.
Lactation and Vitamin C. E. Werner.—p. 2388.
Influence of Estrogenic Hormone on Lactogenic Action of Anterior Lobe of Hypophysis of Lactating Rats. M. Wiegand.—p. 2391.

Radiologic Treatment of Menopausal Hemorrhages.—Von Massenbach reports experiences with roentgen and radium irradiations on women of the menopausal age who were admitted to the clinic on account of hypermenorrhea. He discusses the principles according to which the method of treatment was decided, the dosage of the radium and roentgen irradiations and the results of the treatment. He says that, if curettage revealed a cystic glandular hyperplasia of the uterine mucosa, irradiation was done, provided the woman was past the age of 40. However, if there was only hypermenorrhea and slight or no cystic hyperplasia, irradiation was resorted to only if the woman was more than 45 years old. Regarding the dosage, the author says that amenorrhea is produced by applying to the ovary from 1,800 to 2,000 mg. radium element hours, or 290 roentgens. Treatment with radium is given the preference in patients who have suffered severe loss of blood, because it is most reliable in effecting arrest of the hemorrhage. Roentgen treatment was employed in women in whom an inflammatory process could not be definitely excluded or in whom there existed deformities of the uterine cavity. In comparing roentgen and radium treatment as regards the after-effects, it was found that the former working capacity was reestablished in more than two thirds of the women who had undergone radium treatment but in only about half of the women who had received roentgen treatment. In view of the superiority of the radium treatment in this respect, it was used chiefly in women of the constitutional

type that is subject to symptoms of abolished function, provided of course that inflammatory processes of the adnexa and deformities of the internal surface of the uterus could be excluded.

Wiener Archiv für innere Medizin, Vienna

31: 169-230 (Oct. 31) 1937

Cardiocostal Zones. S. Wassermann.—p. 169.
Genesis of Genopathic Syndrome: Bardet-Biedl Acrocephalosyndactylia. F. L. Pool.—p. 187.
Intravenous Scilla Therapy. L. Zwillinger.—p. 201.
*Diabetes and Vitamin C. R. Pfleger and F. Scholl.—p. 219.

Diabetes and Vitamin C.—Pfleger and Scholl decided to determine how saturation with vitamin C affects the vitamin C metabolism of the carbohydrate metabolism of patients with diabetes mellitus. They accepted elimination in the urine as a measure of complete saturation. They determined the vitamin C deficit by means of the saturation method of Harris. They detected a hypovitaminosis in most diabetic patients: in some the deficit was as high as 2,500 mg. After the normal biologic status had been attained, attempts were made to influence the carbohydrate metabolism. In diabetic patients who were not treated with insulin the cevitamic acid exerted no influence on the sugar content of the blood and urine, but the combustion of the acetone bodies was favorably influenced. After saturation with vitamin C, the action of insulin was noticeably intensified by cevitamic acid, so that the carbohydrate metabolism of the diabetic patients could be regulated with smaller amounts of insulin. In persons without diabetes, saturation with vitamin C did not influence the fasting blood sugar or the blood sugar after tolerance tests. The sugar curves that were obtained after the administration of insulin revealed a noticeable intensification of the insulin effect following saturation with vitamin C. The same effect, although in a milder degree, could be determined in diabetic patients. As explanation of the increased responsiveness to insulin on the part of the organism that is saturated with vitamin C, the authors assume that the cevitamic acid produces an increase in the capacity of liver to assimilate glycogen, or an increase in the tissue metabolism either directly or by activating the insulin. In all diabetic patients, irrespective of the modification of the sugar metabolism, cevitamic acid improves the general condition: the fatigue disappears, the patient feels fresher and the vitality is increased. The authors direct attention to the vitamin C deficiency of the customary diabetic diets and stress the value of the medicinal administration of cevitamic acid.

Problemy Tuberkuleza, Moscow

Pp. 1-135 (No. 7) 1937. Partial Index

Campaign Against Tuberculosis in Course of Third Five Year Plan. S. E. Nezlin, I. I. Lyudvinovskiy and V. S. Koltsman.—p. 3.
*Mechanism of Tuberculin Reactions. L. M. Model.—p. 8.
Alveolar Air in Pulmonary Tuberculosis. E. M. Berkovich.—p. 25.
Paratuberculous Lesions of the Heart. T. D. Kan.—p. 36.
Differential Diagnosis of Grip and of Infiltrating Tuberculous Pneumonia. B. P. Levenshtein and S. I. Gutman.—p. 45.
Demonstration of Bacillemia in Tuberculous Patients. L. Sirotinina.—p. 67.

Mechanism of Tuberculin Reactions.—According to Model, the variations in the sensitivity of an organism to injections of tuberculin are not dependent on the antibody content of the blood. The determining factor is the state and the capacity for reaction of the systems to be stimulated, particularly the nervous-endocrine system. The toxic effect of tuberculin is not limited to a tuberculous organism; it is likewise evident when administered to a healthy organism in large doses. Habituation to the toxic effect of large doses of tuberculin does not indicate the cessation of its toxic effect on parenchymatous organs. Protracted tuberculin action on healthy animals has the effect of first stimulating the functions of the endocrine glands (the thyroid and the adrenals) and later causing degenerative processes. The effect of the tuberculin on the vegetative system is to provoke two types of reaction, that of stimulation and that of depression. Stimulation takes place when the tuberculin activates the function of the thyroid, the adrenals and the vegetative nervous system. Such a reaction has a therapeutic value because it improves the metabolism and cell nutrition and because it accelerates the absorption of inflammatory exudates. The reaction of depression, resulting from the inadequacy of the endocrine glands and of the vegetative nervous system, is expressed in manifestations of intoxication and in the increase of the inflammatory state. As such it has no therapeutic value; on the contrary, it increases the focal inflammatory process, provoking grave subjective symptoms of intoxication. Its effect is to increase, under these conditions, the permeability of the endothelium, to provoke further exudation in the foci, to increase the anoxemia and to diminish the oxidizing processes in the tissues. The review of extensive material from the literature and the author's own observations on children with tuberculous toxemia suggest that tuberculin therapy under certain conditions is capable of exerting a beneficial effect. The observations of ophthalmologists on the favorable effect of careful tuberculin therapy in certain disorders of the conjunctiva and of the eyeball of a tuberculous nature are of particular interest in this connection. Such favorable reactions may be expected in the milder forms of the tuberculous disease. The author emphasizes that in the graver forms of tuberculosis the response to tuberculin takes on a toxic character and aggravates the focal process. He concludes that careful exhibition of tuberculin therapy is permissible in the milder forms of tuberculous processes in the presence of an adequate neuro-endocrine system.

Finska Läkaresällskapets Handlingar, Helsingfors

80: 389-479 (May) 1937

Serologic Diagnosis of Syphilis: Test of Methods Used in Finland. O. Sievers.—p. 395.
Nongonorrheal Urethritis with Joint and Eye Complications: Case. C. Thesleff.—p. 411.
*Tumors of Carotid Gland in Connection with Case in Which Operation was Performed in Finland. C. E. Sonck.—p. 417.
Abscess of Spleen: Case; Contribution to Pathology and Therapy of Splenic Abscess. H. E. Blomquist.—p. 454.

Tumors of Carotid Gland.—Sonck says that this is the first case of carotid tumor to be described from Finland. The tumor was located in the bifurcation of the carotid, had grown about the external carotid and surrounded the internal carotid in a deep groove. Although it could be loosened from the internal carotid, ligation of the external carotid was necessary. No nerves were injured. Recovery was rapid and uneventful and four years after the intervention the patient, a woman, aged 48, continues well. The tumor had been observed for seventeen years, measured 6 by 3.5 by 3 cm., and microscopically was a typical tumor of the carotid gland.

Norsk Magasin for Lægevidenskapen, Oslo

98: 1243-1346 (Oct.) 1937

Suffocation and Inflammation as Occurrences in General Clinical Pathology. G. von Bergmann.—p. 1243.
Value of Havlicek's Application of Ultraviolet Irradiation: Preliminary Clinical Experiences from Division II, Ullevål Hospital, Oslo. S. Widerøe.—p. 1262.
*Hepatolenticular Degeneration (Hall): Case. O. Lingjærde.—p. 1267.
Experimental Investigations on Extent of Anesthesia by Means of Ethyl Chloride. L. Efskind.—p. 1283.
Asthenic Patients: Problem of Asthenia. I. Aasland.—p. 1294.
Psychosis After Insulin Intoxication. B. Helland-Hansen.—p. 1306.
Fibro-Epithelial Tumor, Papilloma, Which Became Sarcoma. O. Berner. —p. 1314.

Hepatolenticular Degeneration (Hall).—Lingjærde's patient, a man aged 22, without family history of hepatolenticular degeneration, had had the disorder for six years. No illness or trauma preceded. The picture was that of Westphal-Strümpell's pseudosclerosis, with heavy tremor of intentional kind, without rigidity, together with dysarthria and psychic symptoms. No pyramidal symptoms were present. There was increased albumin in the cerebrospinal fluid and the mastic curve showed a marked depression. The patient died one month after admission to Rønvik Asylum. Besides a purulent bronchitis and bronchopneumonia, necropsy disclosed typical cirrhosis of the liver and macroscopic changes in the lenticular nuclei. Microscopic examination showed degeneration of the ganglion cells in the brain, especially in the lenticular nuclei on both sides, also in the optic thalamus, medulla oblongata and cerebral cortex, less marked degeneration of the neuroglia cells, with appearance of Alzheimer's cells and Opalski cells, and moderate proliferation of the glia in connection with the blood vessels. Pancreatitis, presumably of recent origin, calcareous deposits in the kidneys, a slight fibrosis of the spleen and perhaps a slight degree of hyperplasia of the parathyroid glands were found. The author thinks that the pancreatitis and the hyperplasia of the parathyroid may have had a part in the rapid exacerbation during the last three months of life.